OMB No. 0990-0115

Electronic Request for Proposal
SOLICITATION COVER PAGE

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Purchase Authority: Public Law 92-218, as amended.
NOTE: The issuance of this solicitation does not commit the government to an award.

RFP Number:	***Just In Time:***	***Small Bus. Set-Aside*** [ ] Yes [X] No ***8(a) Set-Aside*** [ ] Yes [X] No ***NAICS Code: 541710*** ***Size Standard: 500***	***Level of Effort:*** [ ] Yes [X] No ***Total Effort:*** N/A
NIH-NIAID-DAIT-02-11	[ ] Yes [X] No		

TITLE: NIAID Inner-City Asthma Consortium: Immunologic Approaches to Reduce Asthma

Issue Date: June 5, 2001	***Due Date: December 01, 2001*** ***Time: 3:00 P.M. EST.***	***Technical Proposal Page Limits:*** [X] Yes *(see "How to Prepare and Submit Electronic Proposals")* [ ] No

ISSUED BY:

Jacqueline C. Holden
Contracting Officer
Contract Management Branch, DEA
NIH, NIAID
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[ ] ***We reserve the right to make awards without discussion.***

NO. OF AWARDS:

[X] Only 1 Award
[ ] Multiple Awards

PERIOD OF PERFORMANCE:

6 Years beginning on or about August 1, 2002.

Offers will be valid for 120 days unless a different period is specified by the Offeror on the form entitled "Proposal Summary and Data Record, NIH-2043" (See SECTION J - Attachments)

The Official Point of Receipt for the purpose of determining timely delivery is the Contract Management Branch as stated above. If your proposal is not received by the Contracting Officer or Designee at the place and time specified, then it will be considered late and handled in accordance with HHSAR Clause 352.215-70 entitled "Late Proposals and Revisions" located in this Solicitation.

POINT OF CONTACT -- Grace A. Bruce ***--COLLECT CALLS WILL NOT BE ACCEPTED--***

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Updated thru FAC 97-23 (2/20/01)

TABLE OF CONTENTS

BACKGROUND/STATEMENT OF WORK/NOTES TO OFFERORS

[Return to Table of Contents]

BACKGROUND

INTRODUCTION

This Request for Proposals (RFP) details two (2) different components, each with its own work statement.

Part A solicits proposals to establish the Inner-City Asthma Consortium, to design and conduct clinical trials and mechanistic and biomarker studies, in order to reduce severe asthma and prevent asthma among children residing in the inner cities of the United States.

Part B (Option) solicits proposals for expanding the Inner-City Asthma Consortium to encompass studies of the immunopathogenesis of asthma.

Offerors submitting a proposal under this solicitation must prepare a Technical Proposal and a Business Proposal that includes the required work outlined in Part A **AND** a separate Technical Proposal and Business Proposal that includes the required work outlined below in Part B. Proposals for Part A alone or Part B alone will not be accepted for review or considered for award.

It is anticipated that one (1) contract will be awarded to a prime contractor consisting of a network of institutions comprising the Inner-City Asthma Consortium for a period of six (6) years. It is also anticipated that support will be provided for Part A of this solicitation. Support for the activities in Optional Part B of this solicitation may be initiated only when and if (1) additional funds become available; (2) the state of the science warrants implementation; and (3) the Government exercises the OPTION.

Additional Information on the Scope and Requirements of the Solicitation

- Since the study populations for this contract will be exclusively children residing in the inner cities of the United States, only domestic institutions/organizations are eligible to serve as clinical trial sites.

- It is not the intent of the Government to support basic research that does not involve human subjects under this contract. Therefore, Offerors shall not propose fundamental or developmental work on various aspects of immune-based approaches for the treatment of asthma, including animal studies. However, under certain circumstances, the Government and the Consortium will have the flexibility to consider supporting modest fundamental research projects when determined to be important for advancing this clinical research program.

- NIAID will facilitate collaboration and coordination between Consortium investigators and current and planned NIAID-supported research programs in the area of asthma, including the evaluation of new therapeutic approaches in non-human primate models of asthma, the development and validation of assays and biomarkers, and the evaluation of tolerance induction strategies in clinical trials for the treatment of this disease.

- Experimental agents to be evaluated by the Consortium will be provided at no cost to the Contractor. Therefore, Business Proposals shall not include any costs associated with the purchase of investigational agents.

- A broad range of scientific and clinical expertise will be necessary to carry out the requirements of this solicitation. The Government recognizes that no single institution or organization will have the expertise and facilities necessary to perform all requirements and, therefore, it will be necessary for the Prime Contractor to subcontract portions of the work to be performed. A consortium of institutions/organizations is being sought to provide the scientific and clinical expertise necessary to conduct clinical trials and associated mechanistic studies, to develop and validate assays and biomarkers, and to develop critical collaborations between scientific and clinical investigators. Proposals from single institutions or consortia of institutions to conduct only clinical trials, only mechanistic studies, or only assay and biomarker development will not be accepted for review or considered for award. Furthermore, because the design and development path for the research to be carried out under this solicitation cannot be entirely anticipated, a plan for how new scientific findings and new immune-based therapies for asthma will be integrated into the research program will also be required.

- Offerors shall have flexibility in proposing a Consortium structure capable of meeting the requirements of this work statement. The Government anticipates that the Consortium will require strong leadership to provide for the overall scientific

direction, coordination and management of research studies and personnel required. **There will be a Principal Investigator for the Consortium**. Decisions about overall scientific direction, coordination and management of research studies and personnel will be made by the Project Officer in consultation with the Consortium Principal Investigator, and with advice and recommendations from a Consortium Executive Committee made up of clinical investigators and basic scientists. It is likely that the Consortium's leadership, on the Consortium Executive Committee, will require multiple clinical investigators and basic scientists.

- Not more than 25% of the total funds awarded for the contract shall be used for the scientific, clinical, technical, policy and administrative infrastructure required to lead, manage and coordinate the Consortium activities, including the costs of a Consortium central office. Not less than 75% of the total funds awarded for the contract shall be used to support clinical trials, mechanistic studies and biomarker/assay development, including the infrastructure and patient care costs of the clinical trial sites and the mechanistic and biomarker study sites. If the Government exercises the option to implement Part B, the same allocations of the total funds awarded will apply to Part B.

- The Consortium will require flexibility in expanding, curtailing or discontinuing clinical trials, mechanistic studies and/or biomarker studies based on changing priorities and scientific opportunities. All such modifications in the composition of the Consortium shall be proposed by the Consortium Principal Investigator after consulting with the Consortium Executive Committee, which provides advice and recommendations for scientific leadership and direction for overall governance of the Consortium. These modifications will be reviewed by the Project Officer and non-Federal experts, chosen jointly by NIAID and the Consortium Executive Committee, as may be appropriate, and will be approved by the Project Officer.

- The Government recognizes that proposed clinical trials, mechanistic studies and biomarker development can be based only on currently available knowledge and techniques. Therefore, the award of this contract does not commit the Government to approve any of the clinical trials and clinical studies, mechanistic or biomarker studies proposed in the Technical Proposal.

- The NIAID will issue a separate contract to establish a Statistical and Clinical Coordinating Center to provide support to the Consortium in the following areas: (1) design of clinical protocols, including statistical parameters, patient data and patient samples to be collected, etc.; (2) preparation of Investigational New Drug Applications, adherence to regulatory requirements of the U.S. Food and Drug Administration, including reporting of adverse events, clinical site monitoring, assuring the confidentiality of patient data, documentation of Institutional Review Board approval of protocols, etc.; (3) development of procedures for obtaining patient data from clinical sites, establishment and maintenance of a consolidated database for all clinical trials, and data management and quality assurance; (4) analysis of study data; and (5) distribution of investigational agents to clinical sites. One contract, for a period of seven (7) years, will be awarded to establish and maintain the Statistical and Clinical Coordinating Center.

- NIAID will appoint an independent Data and Safety Monitoring Board to advise the NIAID on issues pertaining to the safety and efficacy of investigational agents evaluated in clinical trials supported under this contract, and on other issues concerning the appropriateness of the protocols and the conduct of the clinical trials and clinical studies supported under this contract.

- The NIAID shall review and approve all proposals, clinical protocols, and detailed designs for mechanistic studies and for assay and biomarker development or refinement, and Consortium guidelines, policies and procedures concerning the solicitation, acceptance and evaluation of proposed studies.

- Business Proposals should be prepared based on the scope, requirements and estimates of work provided in this solicitation. However, Offerors must indicate their willingness to use alternative sources of funding. Such alternative sources of funding may include support from biotechnology, pharmaceutical and/or other industrial companies, provided via Clinical Research and Development Agreements (CRADAs) with NIAID or other co-funding mechanisms. The Contractor may also obtain additional funding by submission of a successful grant application to support mechanistic studies accompanying a clinical trial, in response to the NIAID-supported RFA for Hyperaccelerated Award/Mechanisms in Immunomodulation Trials (http://grants.nih.gov/grants/guide/rfa-files/RFA-AI-01-001.html). The Contractor's accounting system must be able to differentiate and track all income and expenditures in order to comply with all applicable cost accounting standards.

BACKGROUND --PART A: CLINICAL TRIALS, MECHANISTIC STUDIES AND BIOMARKER/ ASSAY DEVELOPMENT

Over the past few years, attention has been appropriately focused on the disproportionate burden of asthma on minorities, particularly African-American and Hispanic children residing in the inner city. Since 1991, the National Institute of Allergy and Infectious Diseases (NIAID) has supported research programs to develop effective behavioral, educational and environmental interventions to reduce asthma severity among inner-city children. Major accomplishments of these programs include: (1) the

identification of risk factors for severe asthma that are unique to inner-city children; (2) the development of interventions that effectively reduce asthma severity; and (3) the establishment of clinical research practices that assure community involvement and lead to patient recruitment rates meeting or exceeding enrollment targets and to retention rates of well over 90%. The infrastructure developed within the NIAID-supported inner-city asthma programs and described in publications over the past 10 years represents one successful model for patient recruitment and retention that may be illustrative to potential Offerors for this solicitation.

NIAID continues to place a high priority on reducing the disproportionate burden of asthma by developing effective interventions for children with asthma who live in inner cities. This solicitation is a major component of NIAID's efforts in this area and will establish the Inner-city Asthma Consortium, a network of institutions with the appropriate expertise to: (1) design and conduct clinical trials to evaluate the safety and efficacy of promising immune-based therapies in reducing asthma severity and preventing disease onset in minority children residing in the inner city; (2) design and conduct research to delineate the underlying mechanisms of such therapies as an integral part of the clinical trials undertaken by the Consortium; and (3) develop and validate surrogate/biomarkers to measure disease stage, progression and therapeutic effect.

Over the past two decades, understanding of the pathophysiology and management of asthma has improved significantly, yet the prevalence of this disease has increased by more than 80% in all age and ethnic groups. It is particularly alarming that the death rate from asthma for children ages 5 to 14 doubled from 1980 to 1993. The increasing prevalence and high morbidity from asthma among inner-city children indicate the need for developing new therapies to both reduce asthma severity and prevent disease onset.

The development of new immune-based therapies is a particularly attractive and promising clinical approach. The production of IgE antibody to environmental allergens has been recognized as a hallmark of atopy and allergic diseases. Epidemiological studies have established an association between elevated serum total IgE, asthma, and bronchial hyperresponsiveness; IgE antibody to a subset of allergens, including house dust mite, cockroach and other indoor allergens, is also a consistent finding in asthma. More recently, neonatal exposure to these allergens has been implicated in the development of asthma and allergic diseases. Recent evidence also supports a much broader role of immune system dysfunction in the pathogenesis of asthma. For example, cytokines released from Th2 lymphocytes are involved in the induction and maintenance of airway inflammation, and in regulating IgE and other immune responses. Studies of the genetics of allergic diseases and asthma suggest a strong polygenic component, and candidates for the relevant genes include those that up-regulate the expression of Th2 cytokines and their receptors. It is now thought that the clinical expression of asthma and allergic diseases results from complex interactions involving genes, allergens and other environmental factors**,** such as environmental tobacco smoke and diesel exhaust particulates, which may facilitate the production of IgE. The possibility that infectious agents are involved has also recently been raised.

Immune-based therapies may be particularly valuable for inner-city children with asthma. In these populations, allergen burden is a major contributor to morbidity, as the combination of cockroach allergen exposure and IgE antibodies to allergen is an important risk factor for asthma severity. New classes of drugs that selectively control the allergic component of asthma might avoid the many side effects of corticosteroids. Moreover, patient compliance is often difficult to achieve, particularly in pediatric inner-city populations, and the availability of immune-based therapies with less complicated and less frequent dosing regimens and different side effect profiles might dramatically increase compliance.

Current immune-based approaches to treating asthma focus on reducing allergen exposure or utilizing conventional allergen immunotherapy. Although these therapies have modest therapeutic benefits, there are obstacles to translating these benefits into clinical practice, perhaps because present approaches to environmental control do not sufficiently reduce allergen levels, and because conventional immunotherapy causes only weak modulation of the immune response. New immunologic approaches that potently modulate the immune response may provide more effective therapy for asthma, especially for children in inner cities. These immune-based approaches may also be useful for primary prevention of asthma.

Although primary prevention studies may need to be performed with very young children, intervention studies for primary prevention of asthma would benefit from a new and safer prototype. One possible model is the European preventative allergy treatment (PAT) study, which has recently demonstrated that conventional immunotherapy prevents the development of asthma in children ages 6 and above with allergic rhinoconjunctivitis but not asthma. Prior studies of asthma prevention targeted very young children. However, the results of the PAT study suggest that new immune approaches to prevent asthma could target this population of older children, and such studies would probably be safer than those targeting very young children.

Advances in understanding the cellular and molecular mechanisms underlying the pathogenesis of asthma have led to the identification of a number of potentially useful therapeutic targets within the framework of the immune system, and the pharmaceutical industry has begun to capitalize on these discoveries by developing drugs aimed at these targets. These therapies currently include anti-IgE, anti-IL-5, soluble IL-4 receptor, and allergen-specific DNA or peptide vaccines, currently in phase I, II or III clinical trials, and a number of other drugs in pre-clinical evaluation.

BACKGROUND -PART B: OPTIONAL ACTIVITIES

EXPANSION OF THE INNER-CITY ASTHMA CONSORTIUM: STUDIES OF THE IMMUNE PATHOGENESIS OF ASTHMA

Offerors submitting a proposal under this solicitation must prepare a Technical Proposal and a Business Proposal that includes the required work outlined in Part A **AND** a separate Technical Proposal and Business Proposal that includes the required work outlined below in Part B. Proposals for Part A alone or Part B alone will not be accepted for review or considered for award.

Support for the activities in Optional Part B of this solicitation may be initiated only when and if (1) additional funds become available; (2) the state of the science warrants implementation; and (3) the Government exercises the OPTION.

INTRODUCTION

The pathogenesis of asthma is complex, involving interactions among genes, components of the immune response, environmental factors such as environmental tobacco smoke, and possibly infectious agents. Immune system dysfunction is an important component of asthma pathogenesis. There is strong evidence that IgE antibody production to environmental allergens is relevant to the pathogenesis of atopy and allergic diseases, including asthma, and that excess Th2 cytokine production is upregulated in asthma. Among inner-city children, immune mechanisms are likely to be particularly important. Cockroach allergen exposure appears to be a risk factor for asthma onset, and the combination of cockroach allergen exposure and IgE antibodies to cockroach is a risk factor for asthma severity. Thus, research focusing on the immunologic pathogenesis of asthma should provide important new understanding of asthma in this disproportionately affected population.

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STATEMENT OF WORK

[Return to Table of Contents]

WORK STATEMENT –Part A

Independently and not as an agent of the Government, the Contractor shall furnish all the necessary services, qualified personnel, materials, equipment, and facilities, not otherwise provided by the Government under the terms of this contract, as needed to perform the work set forth below:

The Contractor shall:

1. **Establish the Inner-City Asthma Consortium** (hereinafter referred to as the Consortium), consisting of a network of institutions capable of providing the scientific, clinical, technical and administrative expertise necessary to develop and carry out a long-range scientific plan to reduce asthma severity and prevent asthma among inner-city children. The Consortium shall design and conduct studies to:

    a. Evaluate the short and long-term safety and efficacy of immune-based therapies alone or in combination with other treatments. The trials must be designed either to reduce asthma severity or to prevent asthma onset in children residing in inner cities of the United States.

    b. Delineate the immune mechanisms underlying asthma in these populations as well as the mechanisms of action of the immune-based therapeutic agents.

    c. Refine existing experimental biomarkers/surrogate markers and identify, develop and validate new, potentially useful biomarkers/surrogate markers that can be applied to measuring asthma onset, severity, and response to therapy.

    d. The major focus of the clinical research to be carried out by the Consortium will be on the identification and evaluation of immune-based therapies to reduce asthma severity in inner-city children. To the extent that fundamental knowledge, strategies and investigational agents are available to test approaches to prevent asthma onset in inner-city children at high risk of developing asthma, such approaches shall be considered and, when appropriate, implemented in clinical trials supported by the Consortium.

    e. The patients to be recruited for these studies will be children and adolescents. Studies to reduce asthma severity will be performed with children aged 4-13. Studies to prevent asthma onset may also include children younger than age 4.

    f. For the purpose of this solicitation, “immune-based therapies” are defined as those that achieve their therapeutic effect by altering one or more functions of the pediatric immune system. Such agents include, but are not limited to: agents that target IgE or its receptor; agents that inhibit the actions of IL-4, IL-5, or other cytokines or chemokines; allergen-specific vaccines such as DNA or peptide vaccines; other novel allergen-specific immunotherapeutic agents; and combinations of one or more of these agents, including combinations of antigen-non-specific and antigen-specific agents.

    g. In carrying out these requirements, the Consortium will solicit, accept, evaluate and approve, modify or disapprove proposals for clinical trials, studies of underlying mechanisms, and assay/biomarker development from both Consortium members and non-members. In addition, the Consortium shall develop and implement guidelines, procedures, policies and criteria for the solicitation, review and final decision-making with regard to all proposals for studies to be carried out. Decisions to implement meritorious concepts through the Consortium will be made by the Project Officer in consultation with the Principal Investigator, and with the advice of the Consortium Executive Committee based on scientific merit, feasibility, and the availability of resources during the course of the 6-year contract. All costs associated with the implementation of concepts, whether from Consortium or non-Consortium investigators, will be provided from funds allocated to the 6-year contract.

2. **Develop and implement a plan and organizational structure** for the scientific, technical and administrative

management and coordination of the Consortium, including: (a) priority setting; (b) solicitation, review and approval, modification or disapproval of proposed studies; (c) monitoring and evaluating progress and performance, including augmenting the Consortium with additional organizations and/or institutions as may be necessary to capitalize on new scientific opportunities, adding and discontinuing, temporarily or permanently, the services of subcontractors, and terminating or curtailing ongoing projects; (d) establishing and maintaining effective working relationships and developing partnerships with the pharmaceutical and biotechnology industry and other entities, such as the NIAID-sponsored Immune Tolerance Network, to facilitate the identification of the most promising agents for evaluation in clinical trials; (e) allocation of resources; and (f) redirecting the scientific focus, including the reallocation of resources associated with such redirection.

a. The plan must describe the organizational structure of the Consortium, which will include scientific, technical and administrative staff to direct the activities to be carried out under this contract. At a minimum, the Consortium's organizational structure must include the following:

1) The Consortium Principal Investigator, who will be responsible for the overall leadership, management and coordination of all aspects of the Consortium's activities. The Consortium Principal Investigator must devote at least 25% effort to the contract.

2) The scientific and clinical leadership of the Consortium to include: (1) clinical investigators with expertise and experience in designing and conducting clinical trials in asthma involving inner-city pediatric populations, including the effective recruitment and retention of such study populations; and (2) immunobiologists with expertise in evaluating immunologic approaches to treat or prevent asthma, in designing and carrying out mechanistic studies, and in developing and validating surrogate/biomarkers of disease stage, severity and clinical outcome.

3) The Executive Committee, as scientific and clinical advisors, will provide scientific leadership and direction for the overall governance of the Consortium. The Executive Committee will be chaired by the Principal Investigator and will include approximately 11 members, chosen by the Principal Investigator and approved by the Project Officer. The Committee shall include members with clinical expertise in asthma, especially in inner-city children, and members with expertise in immunobiology. The Project Officer and the Principal Investigator for the Statistical and Clinical Coordinating Center shall both serve as voting members of the Executive Committee.

4) The Executive Committee shall convene three 2-day meetings per year, to be held in the Bethesda, Maryland area, to review governance and fiscal policies and procedures, concepts for clinical trials, mechanistic and biomarker studies, progress of ongoing studies, and future plans. This Committee shall also conduct monthly conference calls in year 1 of this contract, and a minimum of bi-monthly conference calls in years 2-6 of this contract, or more frequently as may be necessary.

5) Other organizational components responsible for the development and implementation of policies and procedures governing (1) the ethical conduct of clinical research involving human subjects; (2) data analysis, publications and the release of information on Consortium activities and study findings; (3) industry and academic liaison; (4) program evaluation; (5) resource allocation (6) mechanistic studies; and (7) assay/biomarker development studies. A representative of each of the organizational components responsible for implementation of these policies and procedures shall participate in a minimum of one 2-day meeting per year, to be held in the Bethesda, Maryland area, in conjunction with one of the Executive Committee meetings; and shall conduct monthly conference calls in year 1 of this contract, and a minimum of bi-monthly conference calls in years 2-6 of this contract, or more frequently as may be necessary.

6) In addition, the Consortium will develop, propose and implement guidelines, policies and procedures regarding conflict of interest on the part of Consortium-supported investigators, including the disclosure of financial interests relevant to the research to be carried out under this contract, that will enable the Consortium to meet the requirements for Federally funded research. These guidelines, policies and procedures will be submitted for approval by NIAID. Consortium-supported investigators will be required to comply with all such policies and procedures.

[SEE NOTES TO OFFEROR: 1, 2, 3, 4]

3. **Develop and implement a scientific plan** to: (1) identify the most promising molecular targets, approaches and agents for clinical evaluation; (2) design clinical trials and integrated studies of underlying mechanisms; and (3)

refine existing or develop new biomarkers and assays. The plan shall include:

a. A discussion of the state-of-the-art of research focused on immune-based therapies for asthma, including factors relevant to the application of such therapies to children residing in the inner city.

b. A description of the knowledge gaps and scientific opportunities relevant for the clinical application of immune-based approaches to reduce asthma severity and prevent disease onset in these populations.

c. A conceptual framework for delineating promising immune-based therapeutic priorities and the rationale for such priorities, including potentially promising agents in development.

d. A description of promising clinical trials, including the rationale for the selection of approaches and overall study design.

e. A conceptual framework for delineating underlying mechanisms through studies conducted as an integral part of the clinical trials undertaken by the Consortium, and a description of promising mechanistic studies, proposed techniques and the overall design of such studies.

f. A conceptual framework for selecting and designing studies of surrogate/biomarkers.

g. A discussion of issues relevant to the testing of experimental therapies in inner-city children with asthma or at high risk of developing asthma, including: (1) the rationale for evaluating new therapeutic approaches in this population; (2) ethical considerations in the design, implementation and monitoring of such clinical trials; and (3) planned strategies and approaches to ensure the effective recruitment and retention of study participants, including a discussion of the obstacles and problems inherent in conducting research in these populations and plans for overcoming such problems and obstacles. The discussion should include protection of human subjects, and specifically protection of children: http://ohrp.osophs.dhhs.gov/humansubjects/guidance/45cfr46.htm; see subpart D, sections 46.401-46.409.

[SEE NOTE TO OFFEROR: 5]

4. **Design and conduct clinical trials** to evaluate the short and long-term safety and efficacy of immune-based therapies alone or in combination with other treatments. The trials must be designed either to reduce asthma severity or to prevent asthma onset in children who live in inner cities in the United States.

a. The major focus of the clinical research to be carried out by the Consortium will be on the identification and evaluation of immune-based therapies to reduce asthma severity in inner-city children. To the extent that fundamental knowledge, strategies and investigational agents are available to test approaches to prevent asthma onset in inner-city children at high risk of developing asthma, such approaches shall be considered and, when appropriate, implemented in clinical trials supported by the Consortium.

b. The Consortium will evaluate only those therapeutic agents whose safety has been adequately demonstrated through clinical trials conducted outside of this contract. Initial studies to establish a safety profile for experimental therapies are not within the scope of this contract.

c. Possible immune-based classes of agents for clinical trials, both to reduce asthma severity and to prevent asthma onset, include, but are not limited to: (a) agents that target IgE or its receptor; (b) agents that inhibit the actions of IL-4, IL-5 or other cytokines or chemokines; (c) allergen-specific vaccines, such as DNA or peptide vaccines; (d) other novel allergen-specific immunotherapeutic agents; and (e) combinations of one or more of these agents, including combinations of antigen-non-specific and antigen-specific agents.

d. Best available current data indicate that: (1) in the first year of this contract, one clinical trial, for six months, at two clinical sites, will be performed, and will involve approximately 200 study participants; (2) in years 2-6 of this contract, up to three clinical trials will be ongoing per year, at a total of approximately five clinical sites per year, and will involve a total of approximately 500 study participants per year.

[SEE NOTES TO OFFEROR: 6, 7]

5. **Design and conduct state of the art mechanistic studies** as an integral part of the clinical trials carried out by the Consortium. Such studies must delineate the mechanisms involved in reducing asthma severity or preventing asthma

onset by the therapeutic agent(s) being evaluated. Possible approaches to obtain data relevant to the study of underlying mechanisms include, but are not limited to, the following.

a. Gene variation analysis to identify differences in patient populations or changes in cellular expression patterns before and after treatment (e.g., DNA technologies, including single nucleotide polymorphism analysis for haplotypes of a single gene, or functional genomic approaches using cDNA microarrays, combined with advanced bioinformatics, to identify differentially expressed genes).

b. Quantitation of IgE levels and FcεRI, FcεRII and other receptors on basophils and other inflammatory cells.

c. Quantitation of Th1 and Th2 subsets (e.g., by Elispot or intracellular cytokine assays).

d. Assessment and/or quantitation of allergen-specific T cells (e.g., by activation marker or intracellular cytokine staining and/or MHC-peptide tetramer staining of epitope-specific T cells).

e. Best available current data indicate that: (1) in the first year of this contract, one laboratory, for six months, will participate in investigations of underlying mechanisms; and (2) in years 2-6 of this contract, approximately three laboratories/year will participate in a total of three studies/year of underlying mechanisms.

[SEE NOTES TO OFFEROR: 8, 9]

6. **Design and conduct assay and biomarker development studies**, associated with the clinical trials, to measure asthma onset, severity, and response to therapy. These studies shall refine existing experimental surrogate/biomarkers and identify, develop and validate new, potentially useful surrogate/biomarkers. These studies will focus on the development and validation of sensitive, reliable and standardized assays capable of measuring the effect of treatment on clinical outcome, and on the use of biomarkers that are: (a) biologically plausible; (b) present early or critical events in the causal pathway; (c) exhibit dose-response effects; and (d) provide accurate measures of pre-and post-treatment disease stage and severity. Possible studies include, but are not limited to: (1) establishing appropriate measures (e.g., cytokines or chemokines and/or their receptors, lymphocyte subsets, other inflammatory cells, etc.); (2) selecting appropriate samples (e.g., blood, urine, biopsies (e.g., skin), lavage (e.g., nasal), etc.); and (3) determining appropriate techniques (e.g., quantitative PCR, microchip technology, imaging, cellular immune assays, etc.) for routine clinical use. Possible markers include: novel cytokines, chemokines or other mediators that regulate inflammation or cell surface proteins; changes in gene or protein expression; or changes in *in vitro* inflammatory cell responsiveness to antigens.

   a. Best available current data indicate that: in years 2-6 of this contract, approximately two laboratories/year will participate in a total of two studies/year of assay/biomarker development and validation.

[SEE NOTES TO OFFEROR: 10]

7. **Provide the appropriate facilities, equipment and resources** to carry out all of the work required under this contract. The Consortium shall also establish shared resources and facilities to provide access to critical scientific and technical support services in a cost-effective manner. For purposes of this solicitation, these resources are referred to as “core resources.”

[SEE NOTES TO OFFERORS: 11, 12]

[END OF STATEMENT OF WORK for Part A]

WORK STATEMENT – PART B OPTION

Independently and not as an agent of the Government, the Contractor shall furnish all the necessary services, qualified personnel, materials, equipment, and facilities, not otherwise provided by the Government under the terms of this contract, as needed to perform the work set forth below:

The Contractor shall:

1. **Expand the Inner-City Asthma Consortium** to provide the scientific, clinical, technical and administrative

expertise necessary to incorporate studies of the immunopathogenesis of asthma. In Part B, the Consortium shall:

a. Design and carry out clinical studies to identify the mechanisms involved in the immunopathogenesis of asthma in inner-city children. These studies shall not involve therapeutic agents. The mechanistic studies shall be the primary focus of Part B.

b. Refine existing experimental biomarkers/surrogate markers and identify, develop and validate new, potentially useful biomarkers/surrogate markers that can be applied to measuring asthma onset and severity.

c. The major focus of the clinical research to be carried out by the Consortium in Part B will be on the immunopathogenesis of asthma in inner-city children who already have the disease. To the extent that fundamental knowledge and strategies are available to perform studies on the immune mechanisms underlying disease onset in inner-city children at high risk of developing asthma, and that such strategies will provide important information about asthma pathogenesis, such approaches shall be considered and, when appropriate, implemented in clinical studies supported by the Consortium under Part B.

d. The patients to be recruited for these studies will be children and adolescents. Studies of the immunopathogenesis of severe asthma will be performed with children aged 4-13. Studies of immunopathogenesis involving children at risk for developing asthma may also include children younger than age 4.

2. **Expand the scientific plan** (Part A, item 3) to: (1) identify the most promising approaches for studies of the immunologic pathogenesis of asthma; (2) design appropriate clinical studies and integrated studies of underlying mechanisms, and (3) refine existing, and/or develop new biomarkers and assays. This plan shall include:

a. A description of state-of-the art research, knowledge gaps and scientific opportunities relevant to immunopathogenesis of asthma, including factors relevant to pathogenesis in inner-city children

b. A conceptual framework for delineating promising clinical studies on immunologic parameters responsible for asthma development, progression, and severity, the rationale for such priorities, the overall study design and proposed techniques.

c. A conceptual framework for selecting and designing studies of surrogate/biomarkers.

d. A discussion of issues relevant to the performing of clinical studies (without therapeutic agents) in inner-city children with asthma or at high risk of developing asthma, including: (1) ethical considerations in the design, implementation and monitoring of such clinical studies; and (2) planned strategies and approaches to ensure the effective recruitment and retention of study participants, including a discussion of the obstacles and problems inherent in conducting research in these populations and plans for overcoming such problems and obstacles.

e. A plan for integrating studies of the immunologic pathogenesis of asthma into the scientific agenda for Part A.

[SEE NOTE TO OFFEROR: 13]

3. **Design and conduct clinical studies** to identify the mechanisms involved in the immunopathogenesis of asthma in inner-city children. These studies shall not involve therapeutic agents. The mechanistic studies shall be the primary focus of Part B.

a. The research studies to be performed in Part B must go beyond correlative studies and focus on the immunologic parameters responsible for asthma development, progression and severity.

b. Possible studies of immunopathogenesis shall include, but are not limited to, the following: (a) relevance of exposure to, and immune responses to, specific allergens; (b) relevance of cytokines produced by Th2 lymphocytes and by other lymphocytes and inflammatory cells; (c) importance of immunologically relevant genes, including those responsible for responsiveness to cockroach and other allergens and those that regulate Th2 cytokine production; (d) relevance of environmental tobacco smoke, diesel exhaust particulates or other air pollutants, alone or in conjunction with allergen; and (e) importance of viral and other infectious agents and immune responses to these infectious agents.

c. The major focus of the clinical research to be carried out by the Consortium in Part B will be on the

immunopathogenesis of asthma in inner-city children who already have the disease. To the extent that fundamental knowledge and strategies are available to perform studies on the immune mechanisms underlying the onset of asthma in inner-city children at high risk of developing asthma, and that such strategies will provide important information about asthma pathogenesis, such approaches shall be considered and, when appropriate, implemented in clinical studies supported by the Consortium under Part B.

d. Possible approaches to obtain data relevant to the study of underlying mechanisms, by analysis of differences between patient populations or within populations over time, include, but are not limited to, the following.

1) Gene variation analysis (e.g., DNA technologies, including single nucleotide polymorphism analysis for haplotypes of a single gene, or functional genomic approaches using cDNA microarrays, combined with advanced bioinformatics, to identify differentially expressed genes).

2) Novel noninvasive bioimaging techniques or imaging agents to measure airways caliber or inflammatory cells in the airways.

3) Quantitation of IgE levels and FcεRI, FcεRII and other receptors on basophils and other inflammatory cells.

4) Quantitation of Th1 and Th2 subsets by Elispot or intracellular cytokine assays.

5) Assessment and/or quantitation of allergen-specific T cells (e.g., activation marker or intracellular cytokine staining and/or MHC-peptide tetramer staining of epitope-specific T cells).

6) Use of these or other studies to characterize asthma phenotypes within the inner-city children's population in relation to underlying immunologic mechanisms.

e. Best available current data indicate that: (1) in years 2 and 3 of the contract, up to two clinical studies/year will be performed at approximately a total of two clinical sites, involving a total of approximately 200 study participants per year, and one mechanistic study site/year will participate; and (2) in years 4-6 of the contract, up to three clinical studies/year will be performed at approximately three clinical sites, involving a total of approximately 300 study participants per year, and approximately two mechanistic study sites/year will participate.

[SEE NOTE TO OFFEROR: 14]

4. **Design and conduct assay and biomarker development studies** to measure asthma onset and severity. These biomarker studies shall refine existing experimental surrogate/biomarkers, and identify, develop and validate new, potentially useful surrogate/biomarkers. Possible studies include, but are not limited to: (1) establishing appropriate measures (e.g., cytokines or chemokines and/or their receptors, lymphocyte subsets, other inflammatory cells, etc.); (2) selecting appropriate samples (e.g., blood, urine, biopsies (e.g., skin), lavage (e.g., nasal), etc.); and (3) determining appropriate techniques (e.g., quantitative PCR, microchip technology, imaging, cellular immune assays, etc.) for routine clinical use. Possible markers include: novel cytokines, chemokines or other mediators that regulate inflammation or cell surface proteins; changes in gene or protein expression; or changes in *in vitro* inflammatory cell responsiveness to antigens.

a. Best available current data indicate that: (1) in years 2-4 of the contract, one biomarker study site/year will participate in one biomarker study; and (2) in years 5-6 of this contract, approximately two biomarker study sites/year will participate in one biomarker study.

[SEE NOTES TO OFFEROR 15, 16]

NOTES TO OFFERORS

[Return to Table of Contents]

NOTES TO OFFEROR FOR PART A

(Note #1 TO OFFEROR)
The Technical Proposal shall include documentation of the qualifications, knowledge, experience,

education, competence, success in designing, implementing, completing and publishing the results of research studies, availability and decision-making skills and authority of the proposed personnel, i.e., (1) the Principal Investigator, (2) Clinical Investigators (3) Immunobiologists. In addition, documentation should be provided for the technical and administrative staff proposed to carry out the requirements of this contract. Documentation shall also include all previous and current projects of a similar nature, including the grant or contract number, the sponsoring agency, the Project Officer, and description of the project. Curricula Vitae of all proposed personnel shall be included in the proposal. In addition, the Offerors shall describe the responsibilities and level of effort of all proposed personnel who will be assigned to the contract, including subcontractors, as well as an administrative framework indicating clear lines of authority. Documentation must include a flow chart illustrating organizational structure and chain of command, operating procedures, timelines, decision-making processes, etc. All costs associated with proposed personnel shall be provided in the Business Proposal.

(Note #2 TO OFFEROR)

Offerors shall include in the Technical Proposal a description of the functions of proposed committees and subcommittees, including the Executive Committee. Offerors shall also include in the Technical Proposal a proposed organization for the governance of the Consortium, including the composition of the Executive Committee.

(Note #3 TO OFFEROR)

The Government anticipates that the organizational structure of the Consortium and plan for the governance of the Consortium, including the functions of committees and subcommittees, including the Executive Committee, can be adequately described in 4-12 pages.

(Note #4 TO OFFEROR)

The Statistical and Clinical Coordinating Center for the Inner-city Asthma Consortium will be responsible for covering the costs of, and handling logistical arrangements for, meetings and conference calls. Therefore, Business Proposals should not include any such costs.

(Note #5 TO OFFEROR)

Offerors shall include in the Technical Proposal a proposed scientific plan. The Government anticipates that a succinct scientific plan of approximately 5-15 pages will be adequate to address this requirement.

The plan should include all of the elements described in Part A, item 3: (a) A discussion of the state-of-the-art of research focused on immune-based therapies for asthma, including factors relevant to the application of such therapies to children residing in the inner city; (b) A description of the knowledge gaps and scientific opportunities relevant for the clinical application of immune-based approaches to reduce asthma severity and prevent disease onset in these populations; (c) A conceptual framework for delineating promising immune-based therapeutic priorities and the rationale for such priorities, including potentially promising agents in development; (d) A description of promising clinical trials, including the rationale for the selection of approaches and overall study design; (e) A conceptual framework for delineating underlying mechanisms through studies conducted as an integral part of the clinical trials undertaken by the Consortium, and a description of promising mechanistic studies, proposed techniques and the overall design of such studies; (f) A conceptual framework for selecting and designing studies of surrogate/biomarkers; and (g) A discussion of issues relevant to the testing of experimental therapies in inner-city children with asthma or at high risk of developing asthma, including: (1) the rationale for evaluating new therapeutic approaches in this population; (2) ethical considerations in the design, implementation and monitoring of such clinical trials; and (3) planned strategies and approaches to ensure the effective recruitment and retention of study participants, including a discussion of the obstacles and problems inherent in conducting research in these populations and plans for overcoming such problems and obstacles

(Note #6 TO OFFEROR)

Offerors should be aware of the requirement to discuss the clinical trials in the scientific agenda component of the Technical Proposal (see note #5 to offeror).

(Note #7 TO OFFEROR)

Offerors shall include in the Technical Proposal protocols for two proposed clinical trials. The Government anticipates that each one of the protocols can be adequately described in a maximum of 15 pages.

The protocols for the clinical trials must include the following: (a) A discussion of the background and significance of the trial; (b) A summary of pre-clinical and clinical data that supports the pursuit of this protocol; (c) A discussion of the rationale for the patient population; (d) statistical calculations and considerations in determining sample size; (e) study design and the therapeutic approach(es) selected for study, including the dose range(s) and timing of the agent(s) to be tested; (f) criteria for inclusion and exclusion of patients; (g) discussion of risks and benefits; and (h) overview of the outcome measures for safety and efficacy. An estimate of direct costs for both proposed clinical trials must be included in the Technical Proposal; these direct costs estimates should not be included in the Business Proposal.

The Government recognizes that proposed clinical trials can be based only on currently available knowledge and techniques. Therefore, the award of this contract does not commit the Government to approve any of the clinical trials proposed in the Technical Proposal.

(Note #8 TO OFFEROR)

Offerors should be aware of the requirement to discuss the mechanistic studies in the scientific agenda component of the Technical Proposal (see note #5 to offeror).

(Note #9 TO OFFEROR)

Offerors shall include in the Technical Proposal two proposed hypothesis-driven mechanistic studies; that is, one mechanistic protocol for each of the proposed clinical trials described in note 7. The Government anticipates that each mechanistic protocol can be adequately described in a maximum of 8 pages. An estimate of direct costs for both proposed mechanistic protocols must be included in the Technical Proposal; these direct costs estimates should not be included in the Business Proposal.

The mechanistic study protocols shall include: (a) A discussion of the background and significance of the proposed study; (b) A discussion of the feasibility, validity, and sensitivity/specificity of the techniques, approaches and markers selected; (c) specific aspects of immune response(s) and function(s) to be measured; (d) a description of the patient samples required, including time and frequency of collection, number and quantity of samples required and methodologies to be used to analyze patient samples; and (e) a discussion of how the results of these studies will contribute to further understanding of asthma and/or of the clinical effects of the therapeutic approaches under investigation.

The Government recognizes that proposed mechanistic studies can be based only on currently available knowledge and techniques. Therefore, the award of this contract does not commit the Government to approve any of the mechanistic studies proposed in the Technical Proposal.

(Note #10 TO OFFEROR)

Offerors should be aware of the requirement to discuss surrogate/biomarker studies in the scientific agenda component of the Technical Proposal (see note #5 to offeror).

(Note #11 TO OFFEROR)

The Technical Proposal must describe the facilities, equipment and resources necessary and available to

carry out the work required under this contract. Offerors may propose the establishment of shared resources and facilities to provide the Consortium with access to critical scientific and technical support services in a cost effective manner. For purposes of this solicitation, these resources are referred to as "core resources." The Technical Proposal shall describe the services to be provided by each proposed core resource and shall discuss the rationale for these services. All costs associated with proposed core resources shall be included in the Business Proposal.

The Government anticipates that the facilities, equipment and resources, including core resources, can be adequately described in 4-12 pages.

(Note #12 TO OFFEROR)

The technical plan for part A of this solicitation shall consist of the components outlined below. In addition to the technical plan, the Offerors shall include in their Technical Proposal appendices consisting of detailed curriculum vitae (no more than 4 pages per individual), and may also include supporting publications, letters of commitment, and relevant subcontractor information.

There is a recommended page limit of 150 pages for the technical proposal for Part A of this solicitation. Technical proposals that exceed this page limit will not be reviewed. Below is a summary table of suggested page limits for the various components of the technical plan, for the Technical Proposal for Part A of this solicitation.

Work Statement Requirement	Note #	Number of pages in the Technical Proposal for an adequate description
1: Establish Consortium		None
2: Plan for Organizational Structure and Governance	3	4-12 pages
3: Scientific Agenda	5	5-15 pages
4: Clinical Trials	7	Two protocols, not to exceed 15 pages each
5: Mechanistic Studies	9	Two protocols (one for each clinical trail), not to exceed 8 pages each
6: Biomarker Studies	10	None (except for description in Scientific Agenda)
7: Facilities, Equipment, Resources	11	4-12 pages
8. Curriculum Vitae	12	No more than 4 pages per individual

NOTES TO OFFEROR FOR PART B

(Note # 13 TO OFFEROR)

Offerors shall include in the Technical Proposal for Part B a description of how the Scientific Plan in Part A will be expanded to incorporate studies of the immunologic pathogenesis of asthma (see note #8 to offeror in Part A). The Government anticipates that discussion of this expanded Scientific Plan can be adequately described in 4-8 pages.

The expanded Scientific Plan shall include all of the elements described in Part B, item 2: (a) A description of state-of-the-art research, knowledge gaps and scientific opportunities relevant to immunopathogenesis of asthma, including factors relevant to pathogenesis in inner-city children; (b) A conceptual framework for delineating promising clinical studies on immunologic parameters responsible for asthma development, progression, and severity, the rationale for such priorities, the overall study design and proposed techniques; (c) A conceptual framework for selecting and designing studies of surrogate/biomarkers; and (d) A discussion of issues relevant to the performing of clinical studies (without therapeutic agents) in inner-city children with asthma or at high risk of developing asthma, including: ethical considerations in

the design, implementation and monitoring of such clinical studies; and planned strategies and approaches to ensure the effective recruitment and retention of study participants, including a discussion of the obstacles and problems inherent in conducting research in these populations and plans for overcoming such problems and obstacles

(Note #14 TO OFFEROR)

Offerors should be aware of the requirement to discuss clinical studies in the expanded Scientific Plan component of the Technical Proposal for Part B (see note #13 to offeror).

Offerors shall also include in the Technical Proposal one proposed protocol for a clinical study of the immunopathogenesis of asthma in inner-city children. The Government anticipates that this protocol can be adequately described in a maximum of 18 pages.

The protocol for the clinical study must include the following: (a) A discussion of the background and significance of the study; (b) A discussion of the rationale for the patient population; (c) Statistical calculations and considerations in determining sample size; (d) Study design; (e) Criteria for inclusion and exclusion of patients; (f) a discussion of risks; (f) A discussion of the feasibility, validity, and sensitivity/specificity of the techniques, approaches and markers selected; (g) The specific aspects of immune response and function to be measured; (h) A description of the patient samples required, including time and frequency of collection, number and quantity of samples required and methodologies to be used to analyze patient samples; and (i) A discussion of how the results of these studies will contribute to further understanding of asthma. An estimate of direct costs for the proposed clinical study must be included in the Technical Proposal; these direct cost estimates should not be included in the Business Proposal.

The Government recognizes that proposed clinical studies can be based only on currently available knowledge and techniques. Therefore, the award of this contract does not commit the Government to approve any of the clinical studies proposed in the Technical Proposal.

(Note #15 TO OFFEROR)

Offerors should be aware of the requirement to discuss the surrogate/biomarker studies in the expanded Scientific Plan component of the Technical Proposal for Part B (see note #13 to offeror). The Technical Proposal for Part B does not require protocols of surrogate/biomarker development and validation.

(Note #16 TO OFFEROR)

The technical plan for Part B of this solicitation shall consist of the components outlined below. In addition to the technical plan, the Offerors shall also include in their Technical Proposal appendices containing information required to expand the contract to encompass Part B, including detailed curriculum vitae of additional personnel for Part B (no more than 4 pages per individual), and may also include supporting publications, letters of commitment, and relevant subcontractor information.

There is a recommended page limit of 50 pages for the technical proposal for Part B of this solicitation. Technical proposals that exceed this page limit will not be reviewed. Below is a summary table of suggested page limits for the various components of the technical plan, for the Technical Proposal for Part B of this solicitation.

Work Statement Requirement	Note #	Number of pages in the Technical Proposal for an adequate description
2: Expand Scientific Plan	13	4-8 pages
3: Clinical Studies	14	One protocol, not to exceed 18 pages
4: Biomarker Studies	15	None (except for description in expanded Scientific Plan)
5. Curriculum Vitae	16	No more than 4 pages per individual

REPORTING REQUIREMENTS AND DELIVERABLES

[Return to Table of Contents]

DELIVERABLES

1. Within sixty (60) days of the award of this contract, the Contractor shall submit an updated plan for clinical research on children with asthma who live in inner cities, including a prioritized list of: (1) agents to be tested in the clinical trials; (2) the overall design of clinical trials; and (3) the overall design of mechanistic and biomarker studies to accompany the clinical trials.

2. Beginning in the fourth month of the first year of this contract, the Contractor shall submit, for NIAID review and approval, proposed concepts for clinical trials, mechanistic studies and biomarker studies to be carried out by the Consortium. Thereafter, proposed concepts for clinical trials, mechanistic studies and biomarker studies shall be submitted quarterly to the NIAID for review and approval.

3. Beginning in the seventh month of the first year of this contract, the Contractor shall submit, for NIAID review and approval, proposed protocols for clinical trials to be conducted by the Consortium, as well as mechanistic and biomarker studies which will be associated with these clinical trials. Thereafter, proposed protocols for clinical trials and for mechanistic and biomarker studies shall be submitted to the NIAID three times a year, as part of the Executive Committee Reports, or more frequently if new opportunities develop.

REPORTING REQUIREMENTS

In addition to those reports listed above, the Contractor shall prepare and submit the following reports in the manner stated below:

There are three types of required progress reports: (1) an Annual Technical Report, (2) Executive Committee Reports to be provided, along with verbal materials, at each of the Executive Committee meetings, to be held three times each year; and (3) a Final Report

All reports shall contain a title page that includes:

Contract number and title
Type of report (Annual, Executive Committee, or Final)
Period of performance being reported
Contractor's name and address
Author(s)
Date of Submission

1. Annual Technical Report

At the completion of each contract year, the Contractor shall submit the Annual Technical Report that summarizes the work accomplished in the preceding twelve month period and outlines work currently in progress. The reports are due on the annual anniversary date of the contract award date. The Annual Technical Report should be factual and concise and consist of the following:

a. SECTION I – The scientific agenda for the Consortium and a brief description of any changes in scientific direction.

b. SECTION II – A section that outlines the status of all identified work tasks from the Statement of Work, Attachment A, and provides a brief description of overall progress, including: (1) approved concepts for clinical trials and mechanistic and biomarker studies; (2) clinical trials and mechanistic and biomarker studies implemented, modified, completed or terminated/curtailed; (3) pertinent interim and final data resulting from clinical trials and mechanistic and biomarker studies; and (4) policies and procedures developed or revised for the overall management and coordination of the Consortium

c. SECTION III – A brief description of all impediments in carrying out the work tasks, whether affecting performance or costs, and recommendations for their resolution.

d. SECTION IV – A brief description of tasks to be completed during the next year and of any difficulties anticipated.

2. Executive Committee Reports

The Executive Committee shall meet three times a year. Two (2) weeks in advance of each of these three annual meetings of the Executive Committee, the Contractor shall provide to the NIAID the following materials: (1) proposed concepts for clinical trials and mechanistic studies; (2) draft clinical protocols and detailed project descriptions for mechanistic and biomarker studies to be carried out based on approved concepts; (3) recommendations for modifications in the scientific agenda of the Consortium, including a description of new knowledge and scientific opportunities, proposals for redirecting scientific and fiscal resources to capitalize on new knowledge and opportunities; (4) a progress report on the status of ongoing clinical trials and mechanistic and biomarker studies, including relevant interim data; (5) results from completed clinical trials and mechanistic and biomarker studies; and (6) recommendations for the modification, expansion, curtailment and/or termination of ongoing studies.

The Contractor shall provide additional verbal progress reports on these topics at the meetings of the Executive Committee for the Consortium.

3. Final Technical Report

At the completion of the contract period, the Contractor shall submit the Final Technical Report summarizing the results of the entire contract work for the complete performance period. The Final Report shall be submitted by the expiration date of the contract and shall be submitted in place of the last Annual Report.

The Final Technical Report shall include: (1) a detailed description of the results of all research conducted under this contract; (2) a scientific agenda to evaluate future research on children with asthma who live in inner cities, including: recommendations for the continuation, expansion or termination of clinical trials and mechanistic and biomarker studies undertaken by the Consortium; new promising therapeutic agents worthy of further investigation; recommendations for the overall design of future clinical trials to evaluate the safety, toxicity and efficacy of such promising new agents; and recommendations for the design of future mechanistic and biomarker studies and promising techniques; and (3) a discussion of problems and obstacles encountered in organizing, managing and coordinating the activities of the Consortium, methods used to overcome problems and obstacles, and recommendations for improvements.

Technical Reports Distribution. Copies of the technical reports shall be submitted according to the schedule below. If the contractor is unable to deliver the reports specified hereunder within the period of performance because of unforeseen difficulties, notwithstanding the exercise of good faith and diligent efforts in performance of the work, the Contractor shall give the Contracting Officer immediate written notice of anticipated delays, stating the reasons.

Type of Report	No. of Copies	Addressee
Executive Committee	2	Program Officer
	1	Contracting Officer Contract Management Branch Division of Extramural Affairs, NIAID National Institutes of Health 6700-B Rockledge Drive Room 2230, MSC 7610 Bethesda, MD 20892-7610
Annual	2	Same as P.O. above
	1	Same as C.O. above
Final	2	Same as P.O. above
	1	Same as C.O. above

TECHNICAL EVALUATION FACTORS FOR AWARD

[Return to Table of Contents]

1. GENERAL

Selection of an Offeror for contract award will be based on an evaluation of proposals against three factors. The factors in order of importance are: Technical, Cost/Price and Small Disadvantaged Business (SDB) Participation. Although technical factors are of paramount consideration in the award of the contract, cost/price and SDB participation are also important to the overall contract award decision. All evaluation factors other than cost or price, when combined, are significantly more important than cost or price. In any case, the Government reserves the right to make an award(s) to that offeror whose proposal provides the best overall value to the Government.

The evaluation will be based on the demonstrated capabilities of the prospective Contractors in relation to the needs of the project as set forth in the RFP. The merits of each proposal will be carefully evaluated. Each proposal must document the feasibility of successful implementation of the requirements of the RFP. Offerors must submit information sufficient to evaluate their proposals based on the detailed criteria listed below.

2. HUMAN SUBJECT EVALUATION

This research project involves human subjects. NIH Policy requires:

(a) **Protection of Human Subjects from Research Risks**

The offeror's proposal must address the involvement of human subjects and protections from research risk relating to their participation, or provide sufficient information on the research subjects to allow a determination by NIAID that a designated exemption is appropriate.

If concerns are identified and you are included in the competitive range, you will be afforded the opportunity to further discuss and/or clarify your position during discussions and in your Final Proposal Revision (FPR). If, after discussions, concerns still exist, your proposal may not be considered further for award.

(b) **Data and Safety Monitoring**

The offeror's proposal must include a general description of the Data and Safety Monitoring Plan for all clinical trials. The principles of data and safety monitoring require that all biomedical and behavioral clinical trails be monitored to ensure the safe and effective conduct of human subjects research, and to recommend conclusion of the trial when significant benefits or risks are identified or if it is unlikely that the trial can be concluded successfully. Risks associated with participation in research must be minimized to the extent practical and the method and degree of monitoring should be commensurate with risk. Additionally, all plans must include procedures for adverse event reporting. Finally, generally, for Phase III clinical trials, the establishment of a Data and Safety Monitoring Board (DSMB) is required, whereas for Phase I and II clinical trials, the establishment of a DSMB is optional. The reviewers should refer to the Statement of Work for the solicitations specific requirements for data and safety monitoring.

The NIAID will evaluate the acceptability of the proposed data and safety monitoring plan with respect to the potential risks to human participants, complexity of study design, and methods for data analysis.

If the information provided about Data and Safety Monitoring is determined to be inadequate, you will be afforded the opportunity to further discuss and/or clarify your plan during discussions and in your Final Proposal Revision (FPR). If, after discussions, the plan is considered inadequate, your proposal may not be considered further for award.

(c) **Women and Minorities**

Women and members of minority groups and their subpopulations must be included in the study population of research involving human subjects, unless a clear and compelling rationale and justification are provided indicating that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. In addition, for Phase III clinical trials, it is required that all proposals and/or protocols provide a description of plans to conduct analyses, as appropriate, to address differences by sex/gender and/or racial/ethnic groups, including subgroups if applicable, unless the

Government has specified in the Statement of Work that this solicitation involves a sex/gender specific study or a single or limited number of minority population groups.

Where the offeror determines that inclusion of women and minority populations is not feasible, a detailed rationale and justification for exclusion of one or both groups from the study population must be submitted with the technical proposal. The NIAID will review the rationale to determine if it is appropriate with respect to the health of the subjects and/or the purpose of the research.

If the rationale is not considered acceptable by the Government and you are included in the competitive range, you will be afforded the opportunity to further discuss, clarify, or modify your plan for inclusion in your Final Proposal Revision (FPR). If your exclusion position is still considered unacceptable by the Government after discussions, your proposal may not be considered further for award.

(d) **Children**

Children (i.e. individuals under the age of 21) must be included in all human subject research unless there are scientific and ethical reasons not to include them.

The offeror's proposal must include a description of plans for including children. If children will be excluded from the research, the proposal must present an acceptable justification for the exclusion. If the offeror determines that exclusion of a specific age range of child is appropriate, the proposal must also address the rationale for such exclusion.

If the information about the inclusion of children is absent or considered inadequate and you are included in the competitive range, you will be afforded the opportunity to further discuss, clarify or modify your plan for inclusion in your Final Proposal Revision (FPR). If your exclusion position is still considered unacceptable by the Government after discussions, your proposal may not be considered further for award.

3. EVALUATION OF OPTIONS

It is anticipated that any contract(s) awarded from this solicitation will contain option provision(s) and period(s).

In accordance with FAR Clause 52.217-5, Evaluation of Options, (July 1990), the Government will evaluate offers for award purposes by adding the total price for all options to the total price for the basic requirement, except when it is determined in accordance with FAR 17.206(b) not to be in the Government's best interests. Evaluation of options will not obligate the Government to exercise the option(s).

4. TECHNICAL EVALUATION CRITERIA

The evaluation criteria are used by the technical evaluation committee when reviewing the technical proposals. Proposals will be judged solely on the written material provided by the Offeror. The criteria below are listed in the order of relative importance with weights assigned for evaluation purposes.

WEIGHT

A. TECHNICAL CAPABILITIES **Points: 55**

1. Effectiveness, Suitability, and Feasibility of the Management Plan: **(10 points)**

Proposed plan for management and coordination of Consortium, including organizational structure, chain of command, operating procedures, timelines, decision-making processes, governance by Executive Committee, and functions of committees and subcommittees, that will provide successful management of the Inner-City Asthma Consortium.

Part A

2. Scientific Rationale, Suitability and Feasibility of: **(20 points)**

   a. Identified knowledge gaps and scientific opportunities for immune-based therapies for asthma, including factors relevant to the application of such therapies to children residing in the inner city
   b. Scientific agenda, including conceptual framework and approaches to clinical trials and to mechanistic and biomarker studies
   c. Identified issues relevant to the testing of experimental therapies in inner-city children with asthma.

3. Scientific Rationale and Feasibility of**: (15 points)**

   a. Protocols for 2 proposed clinical trials
   b. Detailed designs for 2 mechanistic studies, 1 integrated with each proposed clinical trial

Part B

4. Scientific Rationale, Suitability and Feasibility of: (**10 points)**

   a. The proposed plan and approach to expand the Consortium to incorporate clinical studies and biomarker development studies focused on the immunopathogenesis of asthma
   b. The proposed protocol of 1 clinical study

B. PERSONNEL QUALIFICATIONS **Points: 35**

a) Leadership and Management Structure

Proposed scientific, clinical, technical and administrative leadership of the Consortium. This must include the documented training, experience, leadership, and availability of the Principal Investigator, and the competency of the Principal Investigator and surrounding leadership to manage successfully a project of comparable size and complexity.

b) Scientific, Clinical, Technical and Administrative Staff

Documented training, experience, competence and availability of the proposed other professional, technical and administrative staff, documented ability to perform their roles in proposed studies, expertise in similar projects, and the time commitment of the other professional, technical and administrative staff.

c) Subcontractors

Documented training, experience and availability of proposed subcontractor(s), their documented capability to perform the proposed work, expertise in similar projects, and the time commitment proposed.

d) Management of subcontractors

Quality of the scientific plan to identify the need to add, replace, or remove scientific and technical staff of proposed subcontractor(s), dependent on progress or changes in scientific direction.

C. FACILITIES AND RESOURCES **Points: 10**

Documented availability and adequacy of facilities, equipment and resources, including shared resources, necessary to carry out all phases of the proposed project.

TOTAL POINTS **100**

5. EVALUATION OF TARGETS FOR EXTENT OF SMALL DISADVANTAGED BUSINESS PARTICIPATION

SDB participation will not be scored, but the Government's conclusion about overall commitment and realism of the offeror's SDB participation targets will be used in determining the relative merits of the offeror's proposal and in selecting the offeror whose proposal is considered to offer the best value to the Government.

The extent of the offeror's Small Disadvantaged Business (SDB) Participation Targets will be evaluated before determination of the competitive range. Evaluation of SDB participation will be assessed based on consideration of the information presented in the offeror's proposal. The Government is seeking to determine whether the offeror has demonstrated a commitment to use SDB concerns for the work that it intends to perform.

Offers will be evaluated on the following sub-factors:

1) The extent of participation of SDB concerns in terms of the value of the total acquisition.

2) The complexity and variety of the work SDB concerns are to perform. Greater emphasis will be given for arrangements where the SDB shall be performing work appropriate to the scientific objectives expressed in the statement of work.

THE FOLLOWING PAGES CONTAIN A LISTING(S) OF GENERAL CLAUSES WHICH WILL BE APPLICABLE TO MOST CONTRACTS RESULTING FROM THIS RFP. HOWEVER, THE ORGANIZATIONAL STRUCTURE OF THE SUCCESSFUL OFFEROR(S) WILL DETERMINE THE SPECIFIC GENERAL CLAUSES LISTING TO BE CONTAINED IN THE CONTRACT(S) AWARDED FROM THIS RFP.

SECTION I. GENERAL CLAUSES

[Return to Table of Contents]

ARTICLE I.1. GENERAL CLAUSES FOR A COST-REIMBURSEMENT RESEARCH AND DEVELOPMENT CONTRACT - FAR 52.252-2, CLAUSES INCORPORATED BY REFERENCE (FEBRUARY 1998)

This contract incorporates the following clauses by reference, with the same force and effect as if they were given in full text. Upon request, the Contracting Officer will make their full text available. Also, the full text of a clause may be accessed electronically at this address: http://www.arnet.gov/far/.

a. FEDERAL ACQUISITION REGULATION (FAR) (48 CFR CHAPTER 1) CLAUSES:

FAR CLAUSE NO.	DATE	TITLE
52.202-1	Oct 1995	Definitions
52.203-3	Apr 1984	Gratuities (Over $100,000)
52.203-5	Apr 1984	Covenant Against Contingent Fees (Over $100,000)
52.203-6	Jul 1995	Restrictions on Subcontractor Sales to the Government (Over $100,000)
52.203-7	Jul 1995	Anti-Kickback Procedures(Over $100,000)
52.203-8	Jan 1997	Cancellation, Rescission, and Recovery of Funds for Illegal or Improper Activity (Over $100,000)
52.203-10	Jan 1997	Price or Fee Adjustment for Illegal or Improper Activity (Over $100,000)
52.203-12	Jun 1997	Limitation on Payments to Influence Certain Federal Transactions (Over $100,000)
52.204-4	Aug 2000	Printed or Copied Double-Sided on Recycled Paper (Over $100,000)
52.209-6	Jul 1995	Protecting the Government's Interests When Subcontracting With Contractors Debarred, Suspended, or Proposed for Debarment (Over $25,000)
52.215-2	Jun 1999	Audit and Records - Negotiation (Over $100,000)
52.215-8	Oct 1997	Order of Precedence - Uniform Contract Format
52.215-10	Oct 1997	Price Reduction for Defective Cost or Pricing Data
52.215-12	Oct 1997	Subcontractor Cost or Pricing Data (Over $500,000)
52.215-14	Oct 1997	Integrity of Unit Prices (Over $100,000)
52.215-15	Dec 1998	Pension Adjustments and Asset Reversions
52.215-18	Oct 1997	Reversion or Adjustment of Plans for Post-Retirement Benefits (PRB) other than Pensions
52.215-19	Oct 1997	Notification of Ownership Changes

52.215-21	Oct 1997	Requirements for Cost or Pricing Data or Information Other Than Cost or Pricing Data – Modifications
52.216-7	Mar 2000	Allowable Cost and Payment
52.216-8	Mar 1997	Fixed Fee
52.219-8	Oct 1999	Utilization of Small Business Concerns (Over $100,000)
52.219-9	Oct 2000	Small Business Subcontracting Plan (Over $500,000)
52.219-16	Jan 1999	Liquidated Damages - Subcontracting Plan (Over $500,000)
52.222-2	Jul 1990	Payment for Overtime Premium (Over $100,000) (Note: The dollar amount in paragraph (a) of this clause is $0 unless otherwise specified in the contract.)
52.222-3	Aug 1996	Convict Labor
52.222-26	Feb 1999	Equal Opportunity
52.222-35	Apr 1998	Affirmative Action for Disabled Veterans and Veterans of the Vietnam Era
52.222-36	Jun 1998	Affirmative Action for Workers with Disabilities
52.222-37	Jan 1999	Employment Reports on Disabled Veterans and Veterans of the Vietnam Era
52.223-6	Jan 1997	Drug-Free Workplace
52.223-14	Oct 2000	Toxic Chemical Release Reporting
52.225-1	Feb 2000	Buy American Act - Balance of Payments Program - Supplies
52.225-13	Jul 2000	Restrictions on Certain Foreign Purchases
52.227-1	Jul 1995	Authorization and Consent, Alternate I (Apr 1984)
52.227-2	Aug 1996	Notice and Assistance Regarding Patent and Copyright Infringement (Over $100,000)
52.227-11	Jun 1997	Patent Rights - Retention by the Contractor (Short Form) (Note: In accordance with FAR 27.303(a)(2), paragraph (f) is modified to include the requirements in FAR 27.303(a)(2)(i) through (iv). The frequency of reporting in (i) is annual.
52.227-14	Jun 1987	Rights in Data - General
52.232-9	Apr 1984	Limitation on Withholding of Payments
52.232-17	Jun 1996	Interest (Over $100,000)
52.232-20	Apr 1984	Limitation of Cost
52.232-23	Jan 1986	Assignment of Claims
52.232-25	Jun 1997	Prompt Payment
52.232-34	May 1999	Payment by Electronic Funds Transfer--Other Than Central Contractor Registration
52.233-1	Dec 1998	Disputes
52.233-3	Aug 1996	Protest After Award, Alternate I (Jun 1985)
52.242-1	Apr 1984	Notice of Intent to Disallow Costs
52.242-3	Oct 1995	Penalties for Unallowable Costs (Over $500,000)

52.242-4	Jan 1997	Certification of Final Indirect Costs
52.242-13	Jul 1995	Bankruptcy (Over $100,000)
52.243-2	Aug 1987	Changes - Cost Reimbursement, Alternate V (Apr 1984)
52.244-2	Aug 1998	Subcontracts, Alternate II (Aug 1998) *If written consent to subcontract is required, the identified subcontracts are listed in ARTICLE B, Advance Understandings.
52.244-5	Dec 1996	Competition in Subcontracting (Over $100,000)
52.245-5	Jan 1986	Government Property (Cost-Reimbursement, Time and Material, or Labor-Hour Contract)
52.246-23	Feb 1997	Limitation of Liability (Over $100,000)
52.249-6	Sep 1996	Termination (Cost-Reimbursement)
52.249-14	Apr 1984	Excusable Delays
52.253-1	Jan 1991	Computer Generated Forms

b. DEPARTMENT OF HEALTH AND HUMAN SERVICES ACQUISITION REGULATION (HHSAR) (48 CFR CHAPTER 3) CLAUSES:

HHSAR CLAUSE NO.	DATE	TITLE
352.202-1	Jan 2001	Definitions - Alternate I (Apr 1984)
352.228-7	Dec 1991	Insurance - Liability to Third Persons
352.232-9	Apr 1984	Withholding of Contract Payments
352.233-70	Apr 1984	Litigation and Claims
352.242-71	Apr 1984	Final Decisions on Audit Findings
352.270-5	Apr 1984	Key Personnel
352.270-6	Jul 1991	Publication and Publicity
352.270-7	Jan 2001	Paperwork Reduction Act

[End of GENERAL CLAUSES FOR A COST-REIMBURSEMENT RESEARCH AND DEVELOPMENT CONTRACT - Rev. 02/2001].

SECTION J
LIST OF ATTACHMENTS

[Return to Table of Contents]

The following Attachments are provided in full text with this Solicitation:

- Packaging and Delivery of Proposals
- Proposal Intent Response Sheet ***Submit on/before: November 1, 2001***

  Your attention is directed to the "proposal intent response sheet". If you intend to submit a proposal, you must complete this form and return it to this office via fax or e-mail on or before the date identified above. The receipt of this form is critical as it contains information essential for CMB's coordination of the electronic submission and review of proposals.

- How to Prepare and Submit an Electronic Proposal

The RFP Forms/Attachments listed below are available in a variety of formats and may be viewed or downloaded directly from this site. http://www.niaid.nih.gov/contract/ref.htm - 1

Applicable to Technical Proposal

- **Technical Proposal Cover Sheet**
- **Technical Proposal Cost Summary**
- **Summary of Related Activities**
- **Optional Form 310, Protection of Human Subjects Assurance Identification/Certification/Declaration** *[When applicable, all institutions must have the form reviewed and approved by their Institutional Review Committee.]*
- **Government Notice for Handling Proposals**

Applicable to Business Proposal

- **NIH-2043, Proposal Summary and Data Record**
- **Small Business Subcontracting Plan** *[if applicable]*
- **Summary of Proposed Estimated Cost (plus fee) and Labor Hours [with detailed Breakdown of Proposed Costs (Excel cost spreadsheet template)]**
- **Offeror's Points of Contact**

To Become Contract Attachments and Reports Required During Contract Performance (as applicable)

- **Annual Technical Progress Report Format for Each Study** *[Applicable when contract involves Human Subjects unless it has been determined by the Government that the inclusion of Women and Minority Groups in the Study Population is not appropriate.]*
- **NIH(RC)-1: Invoice/Financing Request Instructions for NIH Cost-Reimbursement Type Contracts**
- **NIH(RC)-4: Invoice/Financing Request and Contract Financial Reporting Instructions for NIH Cost-Reimbursement Type Contracts**
- **Procurement of Certain Equipment, NIH(RC)-7 (OMB Bulletin 81-16)**
- **NIH(RC)-11: Research Patient Care Costs**
- **NIH-2706: Financial Report of Individual Project Contract**
- **Instructions for Completing Form NIH-2706**
- **Privacy Act System of Records, #09-25-0200**
- **Safety and Health (Deviation), HHSAR Clause 352.223-70**

HOW TO PREPARE AND SUBMIT AN ELECTRONIC PROPOSAL

[Return to Table of Contents] or [Return to List of Attachments]

Detailed information regarding the electronic process for submission of proposals may be accessed through the CMB Homepage at the following website by clicking on "E-Proposals". http://www.niaid.nih.gov/contract/default.htm

PAGE LIMITS -- THE NARRATIVE PORTION OF THE TECHNICAL PROPOSAL IS LIMITED TO NOT-TO-EXCEED 150 PAGES for Part A and 50 PAGES for Part B. APPENDICES, ATTACHMENTS, OPERATING MANUALS, NON-SCANNABLE FIGURES OR DATA, LETTERS OF INTENT, ETC., SEE NOTES TO OFFERORS FOR RECOMMENDATIONS.

Pages in excess of this will be removed from the proposal and may not be read or evaluated. Offerors are encouraged to limit the overall size of the Technical Proposal (excluding appendices, attachments, operating manuals, non-scannable figures or data, letters of collaboration/intent, etc.). Note that although no page limit has been placed on the Business Proposal, offerors are encouraged to limit its content to only those documents necessary to provide adequate support for the proposed costs.

Type density and size must be 10 to 12 points. If constant spacing is used, there should be no more than 15 cpi, whereas proportional spacing should provide an average of no more than 15 cpi. There must be no more than six lines of text within a vertical inch. Margins must be set to 1 inch around.

GENERAL --- To submit a proposal electronically under this RFP, Offerors will need to prepare the proposal on a word processor or spreadsheet program (for the cost portions) and convert them to Adobe Acrobat Portable Document Format (PDF). THE TECHNICAL PROPOSAL AND BUSINESS PROPOSAL MUST BE CONTAINED ON SEPARATE FILES. Further, to expedite the file transferring process, the two files must be named using the following:

- **Technical Proposal: c:\rfpDAIT0211techprop.pdf**
- **Business Proposal: c:\rfpDAIT0211busiprop.pdf**

If your organization does not have the capability to submit electronically, or unforeseen difficulties occur during transmission, you may submit the electronic copy of your proposal with the original proposal on a diskette, CD-Rom or ZipDisk, in lieu of the internet. The Contract Specialist/Contracting Officer must be notified in advance of using these optional methods.

Approximately TWO weeks prior to the due date of proposals, all offerors will be provided with specific electronic access information and electronic proposal transmission instructions. For this reason, it is imperative that all offerors who are intending to submit a proposal in response to this RFP contact the Contracting Officer identified in this RFP and **complete and submit the attached Proposal Intent Form by the date provided on that Attachment.**.

NOTE: There is no limit to the size (MB) of the two electronic PDF files to be submitted; however, the size of the technical proposal is limited to the page limitation language outlined above. For purposes of assessing compliance with the page count, technical proposals will be viewed using the print function of the Adobe Acrobat Reader, Version 3.0.

ADDITIONAL SUGGESTIONS --- Do not embed sound or video (e.g., MPEG) files into the proposal documents. The evaluation system will not incorporate a capability to read these files. Graphics which are embedded into documents should be kept as simple as possible. Complex graphics require longer periods for the computers used in the evaluation system to draw, and redraw these figures and scrolling through the document is slowed significantly. Suggestions include:

- Limit colors to 256 colors at 1024 x 768 resolution; avoid color gradients.
- Simplify the color palette used in creating figures.
- Be aware of how large these graphics files become. Large files are discouraged.
- Limit scanned images as much as possible.
- Limit appendices and attachments to relevant technical proposal information (e.g., SOPs, pertinent manuals, non-scannable figures or data, resumes, letters of commitment/intent).

PROPOSAL INTENT RESPONSE SHEET

[Return to Table of Contents] or [Return to List of Attachments]

RFP No.: NIH-NIAID-DAIT-021-11
RFP Title: NIAID Inner-City Asthma Consortium: Immunologic Approaches to Reduce Asthma."

Please review the attached Request for Proposal. Furnish the information requested below and return this page by November 1, 2001. Your expression of intent is not binding but will greatly assist us in planning for proposal evaluation.

Since your proposal will be submitted electronically, please include the name and e-mail of the individual to whom the electronic proposal instructions, login code, and password should be provided.

[ ] DO INTEND TO SUBMIT A PROPOSAL
[ ] DO NOT INTEND TO SUBMIT A PROPOSAL FOR THE FOLLOWING REASONS:

Company/Institution Name (print): _____
Address (print): _____
_____
_____
_____

Project Director's Name (print): _____
Title (print): _____
Signature/Date: _____
Telephone Number and E-mail Address (print clearly):
_____
_____

***Name of individual to whom electronic proposal instructions should be sent:**

Name: _____
Title: _____
E-Mail Address: _____
Telephone Number: _____

Names of Collaborating Institutions and Investigators (include Subcontractors and Consultants) (print):
_____
_____
_____
_____
(Continue list on a separate page if necessary)

RETURN VIA FAX OR E-MAIL TO:
CMB, NIAID, NIH
Room 2230
6700-B Rockledge Drive, MSC 7612
Bethesda, MD 20892-7612
Attn: Grace Bruce
RFP-NIH-NIAID-DAIT-02-11
FAX# (301) 402-0972
Email :gb15w@nih.gov

PACKAGING AND DELIVERY OF THE PROPOSAL

[Return to Table of Contents] or [Return to List of Attachments]

[Note to Offeror: Listed below are delivery instructions for the submission of the PAPER copies of your proposal. Instructions for your electronic submission are described above in Electronic Submission Instructions.]

Shipment and marking shall be as indicated below:

A. EXTERNAL PACKAGE MARKING:

In addition to the address cited below, mark each package as follows:

"RFP NO. NIH-NIAID-DAIT-02-11
TO BE OPENED BY AUTHORIZED GOVERNMENT PERSONNEL ONLY"

B. NUMBER OF COPIES:

The number of copies required of each part of your proposal are as specified below.

Technical Proposal: One (1) unbound signed original and 10 unbound copies, with 10 copies of items excluded from electronic submission requirement that you choose to provide in paper format (SOPs, PERTINENT MANUALS, NONSCANNABLE FIGURES OR DATA, AND LETTERS OF COLLABORATION/INTENT.)

Business Proposal: One (1) unbound signed original and 5 unbound copies.

C. PAPER COPIES TO:

If hand delivery or express service	*If using U.S. Postal Service*
Grace A. Bruce Contract Specialist Contract Management Branch, DEA NIAID, NIH 6700-B Rockledge Drive, Room 2230 Bethesda, Maryland 20817	Grace A. Bruce Contract Specialist Contract Management Branch, DEA NIAID, NIH 6700-B Rockledge Drive, Room 2230, MSC 7612 Bethesda, Maryland 20892-7612

NOTE: All material sent to this office by Federal Express should be sent to the Hand Carried Address.

NOTE: The U.S. Postal Service's "Express Mail" does not deliver to the hand delivered (20817 zip code) address. Any package sent to this address via this service will be held at a local post office for pick-up. THE GOVERNMENT IS NOT RESPONSIBLE FOR PICKING UP ANY MAIL AT A LOCAL POST OFFICE. If a proposal is not received at the place, date, and time specified herein, it will be considered a "late proposal," in accordance with PHSAR 352.215-10, Late Proposals, Modifications of Proposals and Withdrawals of Proposals (NOV 1986).

SECTION K

REPRESENTATIONS, CERTIFICATIONS AND OTHER STATEMENTS OF OFFERORS

[Return to Table of Contents]

Representations, Certifications, and Other Statements of Offerors or Quoters (Negotiated).

1. REPRESENTATIONS AND CERTIFICATIONS

The Representations and Certifications required by this particular acquisition can be accessed electronically from the INTERNET at the following address:

http://rcb.nci.nih.gov/forms/rcneg.pdf

If you are unable to access this document electronically, you may request a copy from the Contracting Officer identified on the cover page of this solicitation.

IF YOU INTEND TO SUBMIT A PROPOSAL, YOU MUST COMPLETE THE REPRESENTATIONS AND CERTIFICATIONS AND SUBMIT THEM AS PART OF YOUR BUSINESS PROPOSAL.

SECTION L
INSTRUCTIONS, CONDITIONS AND NOTICES TO OFFERORS

[Return to Table of Contents]

1. GENERAL INFORMATION

a. **INSTRUCTIONS TO OFFERORS--COMPETITIVE ACQUISITION** [FAR Clause 52.215-1 (February 2000)]

(a) Definitions. As used in this provision--

Discussions are negotiations that occur after establishment of the competitive range that may, at the Contracting Officer's discretion, result in the offeror being allowed to revise its proposal.

"In writing" or "written" means any worded or numbered expression which can be read, reproduced, and later communicated, and includes electronically transmitted and stored information.

"Proposal modification" is a change made to a proposal before the solicitation's closing date and time, or made in response to an amendment, or made to correct a mistake at any time before award.

"Proposal revision" is a change to a proposal made after the solicitation closing date, at the request of or as allowed by a Contracting Officer as the result of negotiations.

"Time," if stated as a number of days, is calculated using calendar days, unless otherwise specified, and will include Saturdays, Sundays, and legal holidays. However, if the last day falls on a Saturday, Sunday, or legal holiday, then the period shall include the next working day.

(b) Amendments to solicitations. If this solicitation is amended, all terms and conditions that are not amended remain unchanged. Offerors shall acknowledge receipt of any amendment to this solicitation by the date and time specified in the amendment(s).

(c) Submission, modification, revision, and withdrawal of proposals.

(1) Unless other methods (*e.g.*, electronic commerce or facsimile) are permitted in the solicitation, proposals and modifications to proposals shall be submitted in paper media in sealed envelopes or packages--
  (i) addressed to the office specified in the solicitation;
  (ii) showing the time and date specified for receipt, the solicitation number, and the name and address of the offeror. Offerors using commercial carriers should ensure that the proposal is marked on the outermost wrapper with the information in paragraphs (c)(1)(i) and (c)(1)(ii) of this provision.

(2) The first page of the proposal must show--
  (i) The solicitation number;
  (ii) The name, address, and telephone and facsimile numbers of the offeror (and electronic address if available);
  (iii) A statement specifying the extent of agreement with all terms, conditions, and provisions included in the solicitation and agreement to furnish any or all items upon which prices are offered at the price set opposite each item;
  (iv) Names, titles, and telephone and facsimile numbers (and electronic addresses if available) of persons authorized to negotiate on the offeror's behalf with the Government in connection with this solicitation; and
  (v) Name, title, and signature of person authorized to sign the proposal. Proposals signed by an agent shall be accompanied by evidence of that agent's authority, unless that evidence has been previously furnished to the issuing office.

(3) Submission, modification, revision, and withdrawal of proposals.

  (i) Offerors are responsible for submitting proposals, and any modifications or revisions, so as to reach the Government office designated in the solicitation by the time specified in the solicitation. If no time is specified in the solicitation, the time for receipt is 4:30 p.m., local time, for the designated Government office on the date that proposal or revision is due.
  (ii) (A) Any proposal, modification, or revision received at the Government office designated in the solicitation

after the exact time specified for receipt of offers is "late" and will not be considered unless it is received before award is made, the Contracting Officer determines that accepting the late offer would not unduly delay the acquisition; and--

(*1*) If it was transmitted through an electronic commerce method authorized by the solicitation, it was received at the initial point of entry to the Government infrastructure not later than 5:00 p.m. one working day prior to the date specified for receipt of proposals; or

(*2*) There is acceptable evidence to establish that it was received at the Government installation designated for receipt of offers and was under the Government's control prior to the time set for receipt of offers; or

(*3*) It is the only proposal received.

(B) However, a late modification of an otherwise successful proposal that makes its terms more favorable to the Government, will be considered at any time it is received and may be accepted.

(iii) Acceptable evidence to establish the time of receipt at the Government installation includes the time/date stamp of that installation on the proposal wrapper, other documentary evidence of receipt maintained by the installation, or oral testimony or statements of Government personnel.

(iv) If an emergency or unanticipated event interrupts normal Government processes so that proposals cannot be received at the office designated for receipt of proposals by the exact time specified in the solicitation, and urgent Government requirements preclude amendment of the solicitation, the time specified for receipt of proposals will be deemed to be extended to the same time of day specified in the solicitation on the first work day on which normal Government processes resume.

(v) Proposals may be withdrawn by written notice received at any time before award. Oral proposals in response to oral solicitations may be withdrawn orally. If the solicitation authorizes facsimile proposals, proposals may be withdrawn via facsimile received at any time before award, subject to the conditions specified in the provision at 52.215-5, Facsimile Proposals. Proposals may be withdrawn in person by an offeror or an authorized representative, if the identity of the person requesting withdrawal is established and the person signs a receipt for the proposal before award.

(4) Unless otherwise specified in the solicitation, the offeror may propose to provide any item or combination of items.

(5) Offerors shall submit proposals in response to this solicitation in English, unless otherwise permitted by the solicitation, and in U.S. dollars, unless the provision at FAR 52.225-17, Evaluation of Foreign Currency Offers, is included in the solicitation.

(6) Offerors may submit modifications to their proposals at any time before the solicitation closing date and time, and may submit modifications in response to an amendment, or to correct a mistake at any time before award.

(7) Offerors may submit revised proposals only if requested or allowed by the Contracting Officer.

(8) Proposals may be withdrawn at any time before award. Withdrawals are effective upon receipt of notice by the Contracting Officer.

(d) Offer expiration date. Proposals in response to this solicitation will be valid for the number of days specified on the solicitation cover sheet (unless a different period is proposed by the offeror).

[Note: In accordance with HHSAR 352.215-1, the following paragraph (e) is substituted for the subparagraph (e) of the provision at FAR 52.215-1.]

(e) Restriction on disclosure and use of data. (1) The proposal submitted in response to this request may contain data (trade secrets; business data, e.g., commercial information, financial information, and cost and pricing data; and technical data) which the offeror, including its prospective subcontractor(s), does not want used or disclosed for any purpose other than for evaluation of the proposal. The use and disclosure of any data may be so restricted; provided, that the Government determines that the data is not required to be disclosed under the Freedom of Information Act, 5 U.S.C. 552, as amended, and the offeror marks the cover sheet of the proposal with the following legend, specifying the particular portions of the

proposal which are to be restricted in accordance with the conditions of the legend. The Government's determination to withhold or disclose a record will be based upon the particular circumstances involving the record in question and whether the record may be exempted from disclosure under the Freedom of Information Act. The legend reads:

> Unless disclosure is required by the Freedom of Information Act, 5 U.S.C. 552, as amended, (the Act) as determined by Freedom of Information (FOI) officials of the Department of Health and Human Services, data contained in the portions of this proposal which have been specifically identified by page number, paragraph, etc. by the offeror as containing restricted information shall not be used or disclosed except for evaluation purposes.
>
> The offeror acknowledges that the Department may not be able to withhold a record (data, document, etc.) nor deny access to a record requested pursuant to the Act and that the Department's FOI officials must make that determination. The offeror hereby agrees that the Government is not liable for disclosure if the Department has determined that disclosure is required by the Act.
>
> If a contract is awarded to the offeror as a result of, or in connection with, the submission of this proposal, the Government shall have right to use or disclose the data to the extent provided in the contract. Proposals not resulting in a contract remain subject to the Act.
>
> The offeror also agrees that the Government is not liable for disclosure or use of unmarked data and may use or disclose the data for any purpose, including the release of the information pursuant to requests under the Act. The data subject to this restriction are contained in pages (insert page numbers, paragraph designations, etc. or other identification).

(2) In addition, the offeror should mark each page of data it wishes to restrict with the following statement:

> "Use or disclosure of data contained on this page is subject to the restriction on the cover sheet of this proposal or quotation."

(3) Offerors are cautioned that proposals submitted with restrictive legends or statements differing in substance from the above legend may not be considered for award. The Government reserves the right to reject any proposal submitted with a nonconforming legend.

(f) Contract award.

(1) The Government reserves the right to award a contract or contracts resulting from this solicitation to the responsible offeror(s) whose proposal(s) represents the best value after evaluation in accordance with the factors and subfactors in the solicitation.

(2) The Government may reject any or all proposals if such action is in the Government's interest.

(3) The Government may waive informalities and minor irregularities in proposals received.

(4) The Government intends to evaluate proposals and award a contract without discussions with offerors (except clarifications as described in FAR 15.306(a)). Therefore, the offeror's initial proposal should contain the offeror's best terms from a cost or price and technical standpoint. The Government reserves the right to conduct discussions if the Contracting Officer later determines them to be necessary. If the Contracting Officer determines that the number of proposals that would otherwise be in the competitive range exceeds the number at which an efficient competition can be conducted, the Contracting Officer may limit the number of proposals in the competitive range to the greatest number that will permit an efficient competition among the most highly rated proposals.

(5) The Government reserves the right to make an award on any item for a quantity less than the quantity offered, at the unit cost or prices offered, unless the offeror specifies otherwise in the proposal.

(6) The Government reserves the right to make multiple awards if, after considering the additional administrative costs, it is in the Government's best interest to do so.

(7) Exchanges with offerors after receipt of a proposal do not constitute a rejection or counteroffer by the Government.

(8) The Government may determine that a proposal is unacceptable if the prices proposed are materially unbalanced between line items or subline items. Unbalanced pricing exists when, despite an acceptable total evaluated price, the price of one or more contract line items is significantly overstated or understated as indicated by the application of cost or price analysis techniques. A proposal may be rejected if the Contracting Officer determines that the lack of balance poses an unacceptable risk to the Government.

(9) If a cost realism analysis is performed, cost realism may be considered by the source selection authority in evaluating performance or schedule risk.

(10) The Government may disclose the following information in postaward debriefings to other offerors:

(i) The overall evaluated cost or price and technical rating of the successful offeror;
(ii) The overall ranking of all offerors, when any ranking was developed by the agency during source selection;
(iii) A summary of the rationale for award; and
(iv) For acquisitions of commercial items, the make and model of the item to be delivered by the successful offeror.

Alternate I (October 1997). As prescribed in 15.209(a)(1), substitute the following paragraph (f)(4) for paragraph (f)(4) of the basic provision:

(f) (4) The Government intends to evaluate proposals and award a contract after conducting discussions with offerors whose proposals have been determined to be within the competitive range. If the Contracting Officer determines that the number of proposals that would otherwise be in the competitive range exceeds the number at which an efficient competition can be conducted, the Contracting Officer may limit the number of proposals in the competitive range to the greatest number that will permit an efficient competition among the most highly rated proposals. Therefore, the offeror's initial proposal should contain the offeror's best terms from a price and technical standpoint.

b. **NAICS CODE AND SIZE STANDARD**

Note: The following information is to be used by the offeror in preparing its Representations and Certifications (See Section K of this RFP), specifically in completing the provision entitled, SMALL BUSINESS PROGRAM REPRESENTATION, FAR Clause 52.219-1.

(1) The North American Industry Classification System (NAICS) code for this acquisition is **541710**.

(2) The small business size standard is **500 employees**.

THIS REQUIREMENT IS NOT SET-ASIDE FOR SMALL BUSINESS. However, the Federal Acquisition Regulation (FAR) requires in EVERY solicitation, (except for foreign acquisitions) the inclusion of the North American Industry Classification System (NAICS) Code and corresponding size standard which best describes the nature of the requirement in the solicitation.

c. **NOTICE OF PRICE EVALUATION ADJUSTMENT FOR SMALL DISADVANTAGED BUSINESS CONCERNS**

In accordance with FAR Clause 52.219-23, Notice of Price Evaluation Adjustment for Small Disadvantaged Business Concerns, incorporated in Section I.3., offerors will be evaluated by adding a factor of 10% percent to the price of all offers, except offers from small disadvantaged business concerns that have not waived the adjustment. (Note: A listing of other offerors who are excepted and will not have this evaluation factor added to their offer may be found in subparagraph (b) of FAR Clause 52.219-23.

A small disadvantaged business concern may elect to waive the adjustment, in which case the factor will be added to its offer for evaluation purposes. The agreements in paragraph (d) of FAR Clause 52.219-23 do not apply to offerors that waive the adjustment.

AN OFFEROR WHO ELECTS TO WAIVE THIS EVALUATION ADJUSTMENT MUST SPECIFICALLY INDICATE WITH A STATEMENT TO THIS EFFECT ON THE COVER PAGE OF ITS BUSINESS PROPOSAL.

d. **TYPE OF CONTRACT AND NUMBER OF AWARD(S)**

It is anticipated that ONE AWARD will be made from this solicitation and that the award) will be made on/about August 1, 2002.

It is anticipated that the award from this solicitation will be a multiple-year COST REIMBURSEMENT type COMPLETION contract with a PERIOD OF PERFORMANCE OF SIX (6)YEARS, and that incremental funding will be used [see Section L.2.c. Business Proposal Instructions].

e. **ESTIMATE OF EFFORT**

It is expected that a completion type contract will be awarded as a result of this RFP. To assist you in the preparation of your proposal, the Government considers the total 6 year effort to be approximately as follows:

Part A	
Leadership Group	55%
Clinical Trail Per Site	440%
Mechanistic Study Laboratories Per Site	150%
Biomarker Study Laboratories Per Site	150%
Part B	
Leadership Group	25%
Clinical Trial Per Site	315%
Mechanistic Study Laboratories Per Site	150%
Biomarker Study Laboratories Per Site	150%

. This information is furnished for the offeror's information only and is not to be considered restrictive for proposal purposes.

f. **COMMITMENT OF PUBLIC FUNDS**

The Contracting Officer is the only individual who can legally commit the Government to the expenditure of public funds in connection with the proposed procurement. Any other commitment, either explicit or implied, is invalid.

g. **COMMUNICATIONS PRIOR TO CONTRACT AWARD**

Offerors shall direct all communications to the attention of the Contract Specialist or Contracting Officer cited on the face

page of this RFP. Communications with other officials may compromise the competitiveness of this acquisition and result in cancellation of the requirement.

h. **RELEASE OF INFORMATION**

Contract selection and award information will be disclosed to offerors in accordance with regulations applicable to negotiated acquisition. Prompt written notice will be given to unsuccessful offerors as they are eliminated from the competition, and to all offerors following award.

i. **COMPARATIVE IMPORTANCE OF PROPOSALS**

You are advised that paramount consideration shall be given to the evaluation of technical proposals. All evaluation factors other than cost or price, when combined, are significantly more important than cost or price. The relative importance of the evaluation factors are specified in the TECHNICAL EVALUATION FACTORS FOR AWARD of this solicitation. However, the Government reserves the right to make an award to the best advantage of the Government, cost and other factors considered.

j. **PREPARATION COSTS**

This RFP does not commit the Government to pay for the preparation and submission of a proposal.

k. **SERVICE OF PROTEST** (AUGUST 1996) - FAR 52.233-2

(a) Protests, as defined in section 33.101 of the Federal Acquisition Regulation, that are filed directly with an agency, and copies of any protests that are filed with the General Accounting Office (GAO), shall be served on the Contracting Officer (addressed as follows) by obtaining written and dated acknowledgment of receipt from:

Brenda J. Velez
Chief, Contract Management Branch
National Institutes of Allergies and Infectious Diseases
6700 B Rockledge Dr., Room 2230 MSC 7612
BETHESDA MD 20892-7612

(b) The copy of any protest shall be received in the office designated above within one day of filing a protest with the GAO.

(End of Provision)

l. **LATE PROPOSALS AND REVISIONS, HHSAR 352.215-70**

Notwithstanding the procedures contained in FAR 52.215-1(c)(3) of the provision of this solicitation entitled Instructions to Offerors-Competitive Acquisition, a proposal received after the date specified for receipt may be considered if it offers significant cost or technical advantages to the Government; and it was received before proposals were distributed for evaluation, or within five calendar days after the exact time specified for receipt, whichever is earlier.

(End of provision)

2. INSTRUCTIONS TO OFFERORS [Return to Table of Contents]

a. GENERAL INSTRUCTIONS

INTRODUCTION

The following instructions will establish the acceptable minimum requirements for the format and contents of proposals. Special attention is directed to the requirements for technical and business proposals to be submitted in accordance with these instructions.

(1) **Contract Type and General Clauses**

It is contemplated that a cost-reimbursement, completion type contract will be awarded. (See General Information) Any resultant contract shall include the clauses applicable to the selected offeror's organization and type of contract awarded as required by Public Law, Executive Order, or acquisition regulations in effect at the time of execution of the proposed contract.

(2) **Authorized Official and Submission of Proposal**

The proposal must be signed by an official authorized to bind your organization and must stipulate that it is predicated upon all the terms and conditions of this RFP. Your proposal shall be submitted in the number of copies, to the addresses, and marked as indicated in the Attachment entitled, PACKAGING AND DELIVERY OF PROPOSAL. Proposals will be typewritten, paginated, reproduced on letter size paper and will be legible in all required copies. To expedite the proposal evaluation, all documents required for responding to the RFP should be placed in the following order:

I. COVER PAGE

Include RFP title, number, name of organization, identification of the proposal part, and indicate whether the proposal is an original or a copy.

II. TECHNICAL PROPOSAL

It is recommended that the technical proposal consist of a cover page, a table of contents, and the information requested in the Technical Proposal Instructions.

III. BUSINESS PROPOSAL

It is recommended that the business proposal consist of a cover page, a table of contents, and the information requested in the Business Proposal Instructions.

(3) **Proposal Summary and Data Record (NIH-2043)**

The Offeror must complete the Form NIH-2043, attached, with particular attention to the length of time the proposal is firm and the designation of those personnel authorized to conduct negotiations. (See Attachment entitled, PROPOSAL SUMMARY AND DATA RECORD.)

(4) **Separation of Technical and Business Proposals**

The proposal must be prepared in two parts: a "Technical Proposal" and a "Business Proposal." Each of the parts shall be separate and complete in itself so that evaluation of one may be accomplished independently of, and concurrently with, evaluation of the other. The technical proposal must include direct cost and resources information, such as labor-hours and categories and applicable rates, materials, subcontracts, travel, etc., and associated costs so that the offeror's understanding of the project may be evaluated (See Attachment entitled, TECHNICAL PROPOSAL COST INFORMATION/SUMMARY OF LABOR AND DIRECT COSTS). However, the technical proposal should **not** include pricing data relating to individual salary information, indirect cost rates or amounts, fee amounts (if any), and total costs. The technical proposal should disclose your technical approach in as much detail as possible, including, but not limited to, the requirements of the technical proposal instructions.

(5) **Alternate Proposals**

You may, at your discretion, submit alternate proposals, or proposals which deviate from the requirements; provided, that you also submit a proposal for performance of the work as specified in the statement of work. Such proposals may be considered if overall performance would be improved or not compromised and if they are in the best interests of the Government. Alternative proposals, or deviations from any requirements of this RFP, shall be clearly identified.

(6) **Evaluation of Proposals**

The Government will evaluate technical proposals in accordance with the criteria set forth in the Technical Evaluation Factors for Award.

(7) **Potential Award Without Discussions**

The Government reserves the right to award a contract without discussions if the Contracting Officer determines that the initial prices are fair and reasonable and that discussions are not necessary.

(8) **Use of the Metric System of Measurement**

It is the policy of the Department of Health and Human Services to support the Federal transition to the metric system and to use the metric system of measurement in all procurement, grants, and other business related activities unless such use is impracticable or is likely to cause significant inefficiencies.

The offeror is encouraged to prepare their proposal using either "Hard Metric," "Soft Metric," or "Dual Systems" of measurement. The following definitions are provided for your information:

Hard Metric - The replacement of a standard inch-pound size with an accepted metric size for a particular purpose. An example of size substitution might be: selling or packaging liquids by the liter instead of by the pint or quart (as for soft drinks), or instead of by the gallon (as for gasoline).

Soft Metric - The result of a mathematical conversion of inch-pound measurements to metric equivalents for a particular purpose. The physical characteristics are not changed.

Dual Systems - The use of both inch-pound and metric systems. For example, an item is designed, produced, and described in inch-pound values with soft metric values also shown for information or comparison purposes.

(9) **Human Subjects**

The following notice is applicable when contract performance is expected to involve risk to human subjects:

Notice to Offerors of Requirements of 45 CFR Part 46, Protection of Human Subjects (JANUARY 2001)

a) Copies of the Department of Health and Human Services (Department) regulations for the protection of human subjects, 45 CFR Part 46, are available from the Office for Human Research Protections (OHRP), Office of the Secretary (OS), Department of Health and Human Services (DHHS) – (http://ohrp.osophs.dhhs.gov/index.htm). The regulations provide a systematic means, based on established ethical principles, to safeguard the rights and welfare of individuals who participate as subjects in research activities supported or conducted by the Department.

b) The regulations define a human subject as a living individual about whom an investigator (whether professional or student) conducting research obtains (1) data through intervention or interaction with the individual, or (2) identifiable private information. The regulations extend to the use of human organs, tissue and body fluids from individually identifiable human subjects as well as to graphic, written or recorded information derived from individually identifiable human subjects. The use of autopsy materials is governed by applicable State and local law and is not directly regulated by 45 CFR, Part 46.

c) Activities in which the only involvement of human subjects will be in one or more of the categories set forth in 45 CFR 46.101(b)(1-6) are exempt from coverage.

d) Inappropriate designations of the noninvolvement of human subjects or of exempt categories of research in a project may result in delays in the review of a proposal. The Public Health Service will make a final determination of whether the proposed activities are covered by the regulations or are in an exempt category, based on the

information provided in the proposal. In doubtful cases, prior consideration with OHRP, (telephone: 301-496-7005), is recommended.

e) In accordance with 45 CFR, Part 46, prospective Contractors being considered for award shall be required to file with OHRP an acceptable Assurance of Compliance with the regulations, specifying review procedures and assigning responsibilities for the protection of human subjects. The initial and continuing review of a research project by an institutional review board shall assure that the rights and welfare of the human subjects involved are adequately protected, that the risks to the subjects are reasonable in relation to the potential benefits, if any, to the subjects and the importance of the knowledge to be gained, and that informed consent will be obtained by methods that are adequate and appropriate. Prospective Contractors proposing research that involves human subjects shall be contacted by OHRP and given detailed instructions for establishing an institutional review board and filing an Assurance of Compliance.

f) It is recommended that OHRP be consulted for advice or guidance concerning either regulatory requirements or ethical issues pertaining to research involving human subjects.

(11) **Required Education in the Protection of Human Research Participants**

NIH policy requires education on the protection of human subject participants for all investigators submitting NIH proposals for contracts for research involving human subjects. This policy announcement is found in the NIH Guide for Grants and Contracts Announcement dated June 5, 2000 at the following website: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html. Offerors should review the policy announcement prior to submission of their offers. The following is a summary of the Policy Announcement:

For any solicitation for research involving human subjects, the offeror shall provide in its technical proposal the following information: (1) a list of the names of the principal investigator and any other individuals proposed under the contract who are responsible for the design and/or conduct of the research; (2) the title of the education program completed (or to be completed prior to the award of the contract) for each named personnel; (3) a one sentence description of the program(s) listed in (2) above. This requirement extends to investigators and all individuals responsible for the design and/or conduct of the research who are working as subcontractors or consultants under the contract.

Curricula that are readily available and meet the educational requirement include the NIH on-line tutorial, titled "Protection of Human Research Subjects: Computer-Based Training for Researchers," available at http://ohsr.od.nih.gov/cbt/. This site may be downloaded at no cost and modified for use by the offeror, if desired. In addition, the University of Rochester has made available its training program for individual investigators, and completion of this program will also satisfy the educational requirement. The University of Rochester manual can be obtained through Centerwatch, Inc. at http://www.centerwatch.com/order/pubs_profs_protect.html. If an institution has already developed educational programs on the protection of research participants, completion of these programs will also satisfy the educational requirement.

In addition, prior to the substitution of the principal investigator or any other individuals responsible for the design and/or conduct of the research under the contract, the contractor shall provide the following written information to the contracting officer: the title of the education program and a one sentence description of the program that has been completed by the replacement.

(12) **Inclusion of Women and Minorities in Research Involving Human Subjects**

It is the policy of the NIH that women and members of minority groups and their sub-populations must be included in all NIH-supported biomedical and behavioral research projects involving human subjects, unless a clear and compelling rationale and justification are provided indicating that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43).

All investigators proposing research involving human subjects should read the UPDATED "NIH Guidelines for Inclusion of Women and Minorities as Subjects in Clinical Research," published in the NIH Guide for Grants and Contracts on August 2, 2000 at the following web site:

http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-048.html

A complete copy of the updated Guidelines is available at the following web site:

http://grants.nih.gov/grants/funding/women_min/guidelines_update.htm

The revisions relate to NIH defined Phase III clinical trials and require: a) all proposals and/or protocols to provide a description of plans to conduct analyses, as appropriate, to address differences by sex/gender and/or racial/ethnic groups, including subgroups if applicable; and b) all contractors to report accrual, and to conduct and report analyses, as appropriate, by sex/gender and/or racial/ethnic group differences.

Offerors may obtain copies of the Updated Guidelines from the sources above or from the contact person listed in the solicitation.

Unless otherwise specified in this solicitation, the Government has determined that the work set forth herein does not involve a sex/gender specific study or a single or limited number of minority population groups. Therefore, the NIH believes that the inclusion of women and minority populations is appropriate for this project. (See "Technical Evaluation Factors" of this RFP for more information about evaluation factors for award.)

The format for the Annual Technical Progress Report for Clinical Research Study Populations (See Section J - List of Documents, Exhibits and Other Attachments of this RFP) shall be used in proposal preparation.

(13) **Inclusion of Children in Research Involving Human Subjects**

It is NIH policy that children (defined below) must be included in all human subjects research, including, but not limited to, clinical trials, conducted under a contract funded by the NIH, unless there are scientific or ethical reasons not to include them. For the purposes of this policy, contracts involving human subjects include categories that would otherwise be exempt from the DHHS Policy for Protection of Human Research Subjects (sections 101(b) and 401(b) of 45 CFR 46), such as surveys, evaluation of educational interventions, and studies of existing data or specimens that should include children as participants. This policy applies to both domestic and foreign research contracts.

For purposes of this policy, a child is defined as an individual under the age of 21 years.

Inclusion of children as participants in research must be in compliance with all applicable subparts of 45 CFR 46 as well as other pertinent laws and regulations whether or not such research is otherwise exempted from 45 CFR 46. Therefore, any proposals must include a description of plans for including children, unless the offeror presents clear and convincing justification for an exclusion. In the technical proposal, the offeror should create a section titled "Participation of Children." This section should provide either a description of the plans to include children and a rationale for selecting or excluding a specific age range of child, or an explanation of the reason(s) for excluding children as participants in the research. The RFP will contain a review criterion addressing the adequacy of plans for including children as appropriate for the scientific goals of the research, or justification of exclusion.

All investigators proposing research involving human subjects should read the "NIH Policy and Guidelines on the Inclusion of Children as Participants in Research Involving Human Subjects" which was published in the NIH Guide for Grants and Contracts on March 6, 1998 and is available at the following URL address:

http://www.nih.gov/grants/guide/notice-files/not98-024.html

Offerors may also obtain copies from the contact person listed in the RFP.

(14) **Data and Safety Monitoring in Clinical Trials**

All offerors are directed to the full text of the NIH Policies regarding Data and Safety Monitoring and Reporting of Adverse Events that are found in the NIH Guide for Grants and Contracts Announcements at the following web sites:

http://grants.nih.gov/grants/guide/notice-files/not98-084.html
http://grants.nih.gov/grants/guide/notice-files/not99-107.html
http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html

All offerors receiving an award under this solicitation must comply with the NIH Policy cited in these NIH Announcements and any other data and safety monitoring requirements found elsewhere in this solicitation.

The following is a brief summary of the Data and Safety Monitoring and Adverse Event Reporting Requirements:

Data and Safety Monitoring is required for every clinical trial. Monitoring must be performed on a regular basis and the conclusions of the monitoring reported to the Project Officer.

The type of data and safety monitoring required will vary based on the type of clinical trial and the potential risks, complexity and nature of the trial. A plan for data and safety monitoring is required for all clinical trials. Phase III clinical trials generally require the establishment of a Data Safety Monitoring Board (DSMB). The establishment of a DSMB is optional for Phase I and Phase II clinical trials.

The DSMB/Plan is established at the time the protocol is developed and must be approved by both the Institutional Review Board (IRB) and the Government and in place before the trial begins. If the protocol will be developed under the contract awarded from this solicitation, a general description of the data and safety monitoring plan must be submitted as part of the proposal and will be reviewed by the scientific review group (Technical Evaluation Panel, (TEP)) convened to evaluate the proposal. If the protocol is developed and is included as part of the submitted proposal, a complete and specific data and safety monitoring plan must be submitted as part of the proposal.

Monitoring Plans, at a minimum, must include the prompt reporting of adverse events to the IRB, FDA and NIH. The frequency of reporting of the conclusions of the monitoring activities should also be described in the plan. The overall elements of each plan may vary depending on the size and complexity of the trial. Examples of monitoring activities to be considered are described in the NIH Policy for Data and Safety Monitoring at http://grants.nih.gov/grants/guide/notice-files/not98-084.html

For multi-site Phase I and Phase II trials, a central reporting entity that will be responsible for preparing timely summary reports of adverse events for distribution among sites and IRBs should be considered.

Organizations with a large number of clinical trials may develop standard monitoring plans for Phase I and Phase II trials. In this case, such organizations may include the IRB-approved monitoring plan as part of the proposal submission.

(15) **Reimbursement of Costs for Independent Research and Development Projects (Commercial Organizations Only)**

The primary purpose of the Public Health Service (PHS) is to support and advance independent research within the scientific community. This support is provided in the form of contracts and grants totaling approximately 7 billion dollars annually. PHS has established effective, time tested and well recognized and accepted procedures for stimulating and supporting this independent research by selecting from multitudes of proposals those research projects most worthy of support within the constraints of its appropriations. The reimbursement of independent research and development costs not incidental to product improvement, through the indirect cost mechanism, would circumvent this competitive process.

To ensure that all research and development projects receive similar and equal consideration, all offerors may compete for direct funding for independent research and development projects they consider worthy of support by submitting those projects to the appropriate Public Health Service grant and/or contract office for review. Since these projects may be submitted for direct funding, the successful offeror agrees that no costs for any independent research and development project, including applicable indirect costs, will be claimed under any contract resulting from this solicitation.

(16) **Care of Live Vertebrate Animals**

The following notice is applicable when contract performance is expected to involve care of live vertebrate animals:

Notice to Offerors of Requirement for Adequate Assurance of Protection of Vertebrate Animal Subjects - (SEPTEMBER 1985)

The Public Health Service (PHS) Policy on Human Care and Use of Laboratory Animals establishes a number of requirements for research activities involving animals. Before a PHS award may be made to an applicant organization, the organization shall file, with the Office of Extramural Research (OHRP), Office of Laboratory Animal Welfare (OLAW), National Institutes of Health (NIH), PHS, a written Animal Welfare Assurance which commits the organization to comply with the provisions of the PHS Policy on Humane Care and Use of Laboratory Animals by Awardee Institutions, the Animal Welfare Act, and the Guide for the Care and Use of Laboratory Animals prepared by the Institute of Laboratory Animal Resources. In accordance with the PHS Policy on Humane Care and Use of

Laboratory Animals by Awardee Institutions, applicant organizations must establish a committee, qualified through the experience and expertise of its members, to oversee the institution's animal program, facilities and procedures. No PHS award involving the use of animals shall be made unless the Animal Welfare Assurance has been approved by OER. Prior to award, the Contracting Officer will notify Contractor(s) selected for projects that involve live vertebrate animals that an Animal Welfare Assurance is required. The Contracting Officer will request that OER, OLAW, negotiate an acceptable Animal Welfare Assurance with those Contractor(s). For further information, OER, OLAW, may be contacted at Rockledge Center I – Suite 1050, 6705 Rockledge Drive, Bethesda, MD 20817, (301) 496-7163, ext 234. FAX copies are of the PHS Policy are available at (301) 402-2803. This policy is also available on the internet at http://www.grants.nih.gov/grants/olaw/olaw.htm.

(17) **Privacy Act**

The Privacy Act of 1974 (P.L. 93-579) requires that a Federal agency advise each individual whom it asks to supply information, the authority which authorizes the solicitation, whether disclosure is voluntary or mandatory, the principal purpose or purposes for which the information is intended to be used, the uses outside the agency which may be made of the information, and the effects on the individual, if any, of not providing all or any part of the requested information.

The NIH is requesting the information called for in this RFP pursuant to the authority provided by Sec. 301(a)(7) of the Public Health Service Act, as amended, and P.L. 92-218, as amended.

Providing the information requested is entirely voluntary. The collection of this information is for the purpose of conducting an accurate, fair, and adequate review prior to a discussion as to whether to award a contract.

Failure to provide any or all of the requested information may result in a less than adequate review.

In addition, the Privacy Act of 1974 (P.L. 93-579, Section 7) requires that the following information be provided when individuals are requested to disclose their social security number.

Provision of the social security number is voluntary. Social security numbers are requested for the purpose of accurate and efficient identification, referral, review and management of NIH contracting programs. Authority for requesting this information is provided by Section 301 and Title IV of the PHS Act, as amended.

The information provided by you may be routinely disclosed for the following purposes:

-to the cognizant audit agency and the General Accounting Office for auditing.

-to the Department of Justice as required for litigation.

-to respond to congressional inquiries.

-to qualified experts, not within the definition of Department employees, for opinions as a part of the review process.

(18) **Selection of Offerors**

a) The acceptability of the scientific and technical portion of each research contract proposal will be evaluated by a technical review committee. The committee will evaluate each proposal in strict conformity with the evaluation criteria of the RFP, utilizing point scores and written critiques. The committee may suggest that the Contracting Officer request clarifying information from an offeror.

b) The business portion of each contract proposal will be subjected to a cost and price analysis, management analysis, etc.

c) If award will be made without conducting discussions, offerors may be given the opportunity to clarify certain aspects of their proposal (e.g., the relevance of an offeror's past performance information and adverse past performance information to which the offeror has not previously had an opportunity to respond) or to resolve minor or clerical errors.

d) If the Government intends to conduct discussions prior to awarding a contract-

(1) Communications will be held with offerors whose past performance information is the determining factor preventing them from being placed within the competitive range. Such communications shall address adverse past performance information to which an offeror has not had a prior opportunity to respond. Also, communications may be held with any other offerors whose exclusion from, or inclusion in, the competitive

range is uncertain.

Such communications shall not be used to cure proposal deficiencies or omissions that alter the technical or cost elements of the proposal, and/or otherwise revise the proposal, but may be considered in rating proposals for the purpose of establishing the competitive range.

(2) The Contracting Officer will, in concert with program staff, decide which proposals are in the competitive range. The competitive range will be comprised of all of the most highly rated proposals. Oral or written discussions will be conducted with all offerors in the competitive range.

While it is the Institute's policy to conduct discussions with all offerors in the competitive range, the Institute reserves the right, in special circumstances, to limit the number of proposals included in the competitive range to the greatest number that will permit an efficient competition. All aspects of the proposals are subject to discussions, including cost, technical approach, past performance, and contractual terms and conditions. At the conclusion of discussions, each offeror still in the competitive range shall be given an opportunity to submit a written Final Proposal Revision (FPR) with the reservation of the right to conduct finalization of details with the selected source in accordance with HHSAR 315.370.

e) The process described in FAR 15.101-1 will be employed, which permits the Government to make tradeoffs among cost or price and non-cost factors and to consider award to other than the lowest price offeror or other than the highest technically rated offeror. This process will take into consideration the results of the technical evaluation, the past performance evaluation (if applicable) and the cost analysis.

f) The Institute reserves the right to make a single award, multiple awards, or no award at all to the RFP. In addition, the RFP may be amended or canceled as necessary to meet the Institute’s requirements. Synopses of awards exceeding $25,000 will be published in the Commerce Business Daily.

(19) **Small Business Subcontracting Plan**

If the proposed contract exceeds a total estimated cost of $500,000 for the entire period of performance, the apparent successful offeror shall be required to submit an acceptable subcontracting plan in accordance with the terms of the clause entitled "Small Business Subcontracting Plan," FAR Clause No. 52.219-9, incorporated herein by reference in the Solicitation. SECTION J, LIST OF ATTACHMENTS, to this RFP provides an example of such a plan.

a) **THIS PROVISION DOES NOT APPLY TO SMALL BUSINESS CONCERNS**.

b) The term "subcontract" means any agreement (other than one involving an employer-employee relationship) entered into by a Federal Government prime contractor or subcontractor calling for supplies or services required for the performance of the original contract or subcontract. This includes, but is not limited to, agreements/purchase orders for supplies and services such as equipment purchase, copying services, and travel services.

c) The offeror understands that:

(1) No contract will be awarded unless and until an acceptable plan is negotiated with the Contracting Officer which plan will be incorporated into the contract, as a material part thereof.

(2) An acceptable plan must, in the determination of the Contracting Officer, provide the maximum practicable opportunity for small business concerns and small business concerns owned and controlled by socially and economically disadvantaged persons to participate in the performance of the contract.

(3) If a subcontracting plan acceptable to the Contracting Officer is not negotiated within the time limits prescribed by the contracting activity and such failure arises out of causes within the control and with the fault or negligence of the offeror, the offeror shall be ineligible for an award. The Contracting Officer shall notify the Contractor in writing of the reasons for determining a subcontracting plan unacceptable early enough in the negotiation process to allow the Contractor to modify the plan within the time limits prescribed.

(4) Prior compliance of the offeror with other such subcontracting plans under previous contracts will be considered by the Contracting Officer in determining the responsibility of the offeror for award of the contract.

(5) It is the offeror's responsibility to develop a satisfactory subcontracting plan with respect to small business concerns and small business concerns owned and controlled by socially and economically disadvantaged

individuals, and women-owned small business concerns, and that each such aspect of the offeror's plan will be judged independent of the other.

(6) The offeror will submit, as required by the Contracting Officer, subcontracting reports in accordance with the instructions thereon, and as further directed by the Contracting Officer. Subcontractors will also submit these reports to the Government's Contracting Officer or as otherwise directed, with a copy to the prime Contractor's designated small and disadvantaged business liaison.

d) Each plan must contain the following:

(1) Goals, expressed in terms of percentages of total planned subcontracting dollars, for the use of Small, small disadvantaged, women-owned, and HUBZone small business concerns as subcontractors.

(2) A statement of total dollars planned to be subcontracted. A statement of total dollars to be subcontracted to each of the following type of small business concerns: Small, Small Disadvantaged, Women-Owned, and HUBZone Small Businesses.

(3) A description of the principal types of supplies and services to be subcontracted with an identification of which supplies and services are expected to be subcontracted to small, small disadvantaged, women-owned and/or HUBZone small business concerns.

(4) A description of the method used to develop the subcontracting goals.

(5) A description of the method used to identify potential sources for solicitation purposes.

(6) A statement as to whether or not indirect costs were included in establishing subcontracting goals. If they were, a description of the method used to determine the proportionate share of indirect costs to be incurred with small, small disadvantaged, women-owned, and HUBZone small business concerns.

(7) The name of the individual employed by the offeror who will administer the offeror's subcontracting program and a description of his/her duties.

(8) A description of the efforts the offeror will make to assure that small, small disadvantaged, women-owned, and HUBZone small business concerns have an equitable chance to compete for subcontracts.

(9) Assurances that the offeror will include in all subcontracts the contract clause "Utilization of Small Business Concerns." Assure that all subcontractors, other than small businesses, in excess of $500,000 adopt a plan similar to the plan agreed upon by the offeror.

(10) Assurances that the offeror (and any required subcontractors) will cooperate in studies or surveys as required and submit required reports (SF 294 and SF 295) to the Government.

(11) List the types of records the offeror will maintain to demonstrate procedures that have been adopted to comply with the requirement and goals in the plan, including establishing source lists. Also, the offeror shall describe its efforts to locate small, small disadvantaged, women-owned, and HUBZone small business concerns and award subcontracts to them.

For additional information about each of the above elements required to be contained the subcontracting plan, see FAR Clause 52.219-9, Small Business Subcontracting Plan, and the Sample Subcontracting Plan which is provided as an attachment to this RFP in SECTION J.

(20) **HUBZone Small Business Concerns**

Small Business offerors located in underutilized business zones, called "HUBZones," will be evaluated in accordance with FAR Clause 52.219-4, NOTICE OF PRICE EVALUATION PREFERENCE FOR HUBZONE SMALL BUSINESS CONCERNS, which is incorporated by reference in ARTICLE I.3. of this solicitation. Qualified HUBZone firms are identified in the Small Business Administration website at http://www.sba.gov/hubzone.

(21) **Extent of Small Disadvantaged Business Participation**

In accordance with FAR Subpart 15.304(c)(4), the extent of participation of Small Disadvantaged Business (SDB) concerns in performance of the contract in the authorized NAICS Industry Subsectors shall be evaluated in unrestricted competitive acquisitions expected to exceed $500,000 ($1,000,000 for construction) subject to certain limitations (see FAR 19.1202-1 and 19.1202-2(b). The dollar amounts cited above include any option years/option quantities that may be included in this solicitation. The definition of a "small disadvantaged business" is cited in FAR 19.001.

The factor entitled “Extent of Small Disadvantaged Business Participation” as set forth under the **Technical Evaluation Criteria**, shall be used for evaluation purposes. Credit under this evaluation factor is not available to SDB concerns that receive a Price Evaluation Adjustment (PEA) under FAR 19.11. Therefore, an SDB will be evaluated on this factor only if that SDB concern waives the PEA. **Waiver of the price evaluation adjustment shall be clearly stated in the proposal.**

The Department of Commerce determines, on an annual basis, by Subsectors, as contained in the North American Industry Classification System (NAICS) codes, and region, if any, the authorized SDB procurement mechanisms and applicable factors (percentages). The NAICS codes can be found at: http://www.sba.gov/size/NAICS-cover-page.htm

The Department of Commerce website for the annual determination is:
http://www.arnet.gov/References/sdbadjustments.htm

Offerors shall include with their offers, SDB targets, expressed as dollars and percentages of total contract value, in each of the applicable, authorized NAICS Industry Subsector(s). **The applicable authorized NAICS Subsector(s) for this project is (are) identified elsewhere in this RFP.** A total target for SDB participation by the prime contractor, that includes any joint ventures and team members, shall be provided as well as a total target for SDB participation by subcontractors. In addition, offerors must provide information that describes their plans for meeting the targets set forth in their proposal. **This information shall be provided in one clearly marked section of the Business Proposal, which shall describe the extent of participation of SDB concerns in the performance of the contract.**

If the evaluation factor in this solicitation includes an SDB evaluation factor or subfactor that considers the extent to which SDB concerns are specifically identified, the SDB concerns considered in the evaluation shall be listed in any resultant contract. Offerors should note that addressing the extent of small disadvantaged business participation **is not in any way intended to be a substitute** for submission of the subcontracting plan, if it is required by this solicitation. An example of the type of information that might be given (in addition to the narrative describing the plan for meeting the targets) follows:

EXAMPLE

Targets for SDB Participation - NAICS Industry Subsector 87

	SDB Percentage of Total Contract Value	**SDB Dollars**
Total Contract Value- $1,000,000	25%	$250,000
SDB Participation by Prime	10%	$100,000
(Includes joint venture partners and team arrangements)*		
SDB Participation by subcontractors	15%	$150,000

*Note: FAR Subpart 9.6 defines “Contractor team arrangements” to include two or more companies forming a partnership or joint venture to act as a potential prime contractor, or a potential prime contractor who agrees with one or more companies to have them act as its subcontractors on a specific contract or acquisition program. For purposes of evaluation of the SDB participation factor, FAR 19.1202-4 requires that SDB joint ventures and teaming arrangements at the prime level be presented separately from SDB participation by subcontractors.

(22) **Salary Rate Limitation in Fiscal Year 2001***

Offerors are advised that pursuant to P.L. 106-554, no NIH Fiscal Year 2001 (October 1, 2000 - September 30, 2001) funds may be used to pay the direct annual salary of an individual through any contract awarded as a result of this solicitation at a rate in excess of the Executive Schedule, Level I* (direct salary is exclusive of Overhead, Fringe

Benefits and General and Administrative expenses, also referred to as "indirect cost" or "facilities and administrative (F&A) costs"). Direct salary has the same meaning as the term "institutional base salary." An individual's direct salary (or institutional base salary) is the annual compensation that the contractor pays for an individual's appointment whether that individual's time is spent on research, teaching, patent care or other activities. Direct salary (or institutional base salary) excludes any income that an individual may be permitted to earn outside of duties to the contractor.).

This does not preclude the offeror from absorbing that portion of an employee's annual salary (plus the dollar amount for fringe benefits and associated indirect costs) that exceeds a rate of the Executive Schedule, Level I*. The salary rate limitation set by P.L. 106-554 applies only to Fiscal Year 2001 funds, however, salary rate ceilings for subsequent years may be included in future DHHS appropriation acts. Multi-year contracts awarded pursuant to this solicitation may be subject to unilateral modifications by the Government if an individual's annual salary exceeds any salary rate ceiling established in future appropriations acts. The Executive Schedule, Level I* annual salary rate limit also applies to individuals proposed under subcontracts, however it does not apply to consultants. P.L. 106-554 states in pertinent part:

> "None of the funds appropriated in this Act for the National Institutes of Health and the Substance Abuse, and Mental Health Services Administration shall be used to pay the salary of an individual through a grant or extramural mechanism at a rate in excess of Executive Level I."

***This rate may change periodically. For your information, the rate can be found at: http://www3.opm.gov/oca/01tables/execses/html/01execsc.htm**

(23) **Institutional Responsibility Regarding Conflicting Interests of Investigators**

EACH INSTITUTION MUST:

(a) Maintain an appropriate written, enforced policy on conflict of interest that complies with 42 CFR Part 50 Subpart F and/or 45 CFR Part 94 as appropriate and inform each investigator of the Institution's policy, the Investigator's reporting responsibilities, and the applicable regulations. If the Institution carries out the NIH funded research through subgrantees, contractors or collaborators, the Institution must take reasonable steps to ensure that Investigators working for such entities comply with the regulations, either by requiring those investigators to comply with the Institution's policy or by requiring the entities to provide assurances to the Institution that will enable the Institution to comply with the regulations.

(b) Designate an Institutional official(s) to solicit and review financial disclosure statements from each Investigator who is planning to participate in NIH-funded research.

(c) Require that by the time an application/proposal is submitted to the NIH each investigator who is planning to participate in the NIH-funded research has submitted to the designated official(s) a listing of his/her known Significant Financial Interests (and those of his/her spouse and dependent children): (i) that would reasonably appear to be affected by the research for which the NIH funding is sought; and (ii) in entities whose financial interests would reasonably appear to be affected by the research. All financial disclosures must be updated during the period of the award, either on an annual basis or as new reportable Significant Financial Interests are obtained.

(d) Provide guidelines consistent with the regulations for the designated official(s) to identify conflicting interests and take such actions as necessary to ensure that such conflicting interests will be managed, reduced, or eliminated.

(e) Maintain records, identifiable to each award, of all financial disclosures and all actions taken by the institution with respect to each conflicting interest for: (1) in the case of grants, at least three years from the date of submission of the final expenditures report or, where applicable, from other dates specified in 45 CFR Part 74.53(b) and (2) in the case of contracts, 3 years after final payment or, where applicable, for the other time period specified in 48 CFR Part 4 Subpart 4.7, Contract Records Retention.

(f) Establish adequate enforcement mechanisms and provide for sanctions where appropriate.

(g) Certify, in each application/proposal for funding to which the regulations applies, that:

1) there is in effect at the Institution a written and enforced administrative process to identify and manage, reduce or eliminate conflicting interests with respect to all research projects for which funding is sought from the NIH;

2) prior to the Institution's expenditure of any funds under the award, the Institution will report to the awarding component the existence of a conflicting interest (but not the nature of the interest or other details) found by the Institution and assure that the interest has been managed, reduced or eliminated in accord with the regulations; and for any interest that the Institution identifies as conflicting subsequent to the expenditure of funds after award, the report will be made and the conflicting interest managed, reduced, or eliminated, at least on a temporary basis within sixty days of that identification;

3) the Institution agrees to make information available, upon request, to the awarding component regarding all conflicting interests identified by the Institution and how those interested have been managed, reduced, or eliminated to protect the research from bias; and

4) the Institution will otherwise comply with the regulations.

Institutional Management of Conflicting Interests

(a) The designated official(s) must: (1) review all financial disclosures; and (2) determine whether conflict of interest exists, and if so, determine what actions should be taken by the Institution to manage, reduce or eliminate such conflict of interest. **A conflict of interest exists when the designated official(s) reasonably determines that a Significant Financial Interest could directly and significantly affect the design, conduct, or reporting of the NIH-funded research**.

Examples of conditions or restrictions that might be imposed to manage actual or potential conflicts of interests include, but are not limited to:

(i) public disclosure of significant financial interests;
(ii) monitoring of research by independent reviewers;
(iii) modification of the research plan;
(iv) disqualification of the Investigator(s) from participation in all or a portion of the research funded by the awarding component;
(v) divestiture of significant financial interests; or
(vi) severance of relationships that create actual or potential conflicts of interests.

(b) An Institution may require the management of other conflicting financial interests in addition to those described in paragraph (a) of this section, as the Institution deems appropriate.

(24) **ROTC Access and Federal Military Recruiting on Campus**

Section 514 of the FY 1997 Appropriations Act prohibits NIH from providing contract funds to educational institutions that the Secretary of Defense determines have a policy or practice (regardless of when implemented) that either prohibits, or in effect prevents (1) the maintaining, establishing, or operation of a unit of the Senior Reserve Officer Training Corps at the covered education entity; or (2) a student at the covered educational entity from enrolling in a unit of the Senior Reserve Officer Training Corps at another institution of higher education.

Further, contract funds may not be provided to educational institutions that have a policy or practice that prohibits or prevents (1) entry to campuses, or access to students (who are 17 years of age or older) on campuses, for purposes of Federal military recruiting; or (2) access by military recruiters for purposes of Federal military recruiting to information pertaining to students (who are 17 years of age or older) enrolled at the covered educational entity.

(25) **Solicitation Provisions Incorporated by Reference,** FAR 52.252-1 (February 1998)

This Solicitation incorporates one or more solicitation provisions by reference, with the same force and effect as if they were given in full text. Upon request, the Contracting Officer will make their full text available. The offeror is cautioned that the listed provisions may include blocks that must be completed by the offeror and submitted with its quotation or offer. In lieu of submitting the full text provisions, the offeror may identify the provision by paragraph identifier and provide the appropriate information with its quotation or offer. Also, the full text of a solicitation provision may be accessed electronically at this address: http://www.arnet.gov/far/.

FEDERAL ACQUISITION REGULATION (48 CFR CHAPTER 1):

a) Facilities Capital Cost of Money, FAR Clause 52.215-16, (October 1997).
b) Order of Precedence-Uniform Contract Format, FAR Clause 52.215-8, (October 1997).
c) Preaward On-Site Equal Opportunity Compliance Evaluation, (Over $10,000,000), FAR Clause 52.222-24, (February 1999).

b. TECHNICAL PROPOSAL INSTRUCTIONS [Return to Table of Contents]

A detailed work plan must be submitted indicating how each aspect of the statement of work is to be accomplished. Your technical approach should be in as much detail as you consider necessary to fully explain your proposed technical approach or method. The technical proposal should reflect a clear understanding of the nature of the work being undertaken. The technical proposal must include information on how the project is to be organized, staffed, and managed. Information should be provided which will demonstrate your understanding and management of important events or tasks.

(1) **Technical Discussions**

The technical discussion included in the technical proposal should respond to the items set forth below:

a) **Statement of Work**

(1) Objectives

State the overall objectives and the specific accomplishments you hope to achieve. Indicate the rationale for your plan, and relation to comparable work in progress elsewhere. Review pertinent work already published which is relevant to this project and your proposed approach. This should support the scope of the project as you perceive it.

(2) Approach

Use as many subparagraphs, appropriately titled, as needed to clearly outline the general plan of work. Discuss phasing of research and, if appropriate, include experimental design and possible or probable outcome of approaches proposed.

(3) Methods

Describe in detail the methodologies you will use for the project, indicating your level of experience with each, areas of anticipated difficulties, and any unusual expenses you anticipate.

(4) Schedule

Provide a schedule for completion of the work and delivery of items specified in the statement of work. Performance or delivery schedules shall be indicated for phases or segments, as applicable, as well as for the overall program. Schedules shall be shown in terms of calendar months from the date of authorization to proceed or, where applicable, from the date of a stated event, as for example, receipt of a required approval by the Contracting Officer. Unless the request for proposal indicates that the stipulated schedules are mandatory, they shall be treated as desired or recommended schedules. In this event, proposals based upon the offeror's best alternative schedule, involving no overtime, extra shift or other premium, will be accepted for consideration.

b) **Personnel**

Describe the experience and qualifications of personnel who will be assigned for direct work on this program. Information is required which will show the composition of the task or work group, its general qualifications, and recent experience with similar equipment or programs. Special mention shall be made of direct technical supervisors and key technical personnel, and the approximate percentage of the total time each will be available for this program.

OFFERORS SHOULD ASSURE THAT THE PRINCIPAL INVESTIGATOR, AND ALL OTHER PERSONNEL PROPOSED, SHALL NOT BE COMMITTED ON FEDERAL GRANTS AND CONTRACTS FOR MORE THAN A TOTAL OF 100% OF THEIR TIME. IF THE SITUATION ARISES WHERE IT IS DETERMINED THAT A PROPOSED EMPLOYEE IS COMMITTED FOR MORE THAN 100% OF HIS OR HER TIME, THE GOVERNMENT WILL REQUIRE ACTION ON THE PART OF THE OFFEROR TO CORRECT THE TIME COMMITMENT.

(1) Principal Investigator/Project Director

List the name of the Principal Investigator/Project Director responsible for overall implementation of the contract and key contact for technical aspects of the project. Even though there may be co-investigators, identify the Principal Investigator/Project Director who will be responsible for the overall implementation of any awarded contract. Discuss the qualifications, experience, and accomplishments of the Principal Investigator/Project Director. State the estimated time to be spent on the project, his/her proposed duties, and the areas or phases for which he/she will be responsible.

(2) Other Investigators

List all other investigators/professional personnel who will be participating in the project. Discuss the qualifications, experience, and accomplishments. State the estimated time each will spend on the project, proposed duties on the project, and the areas or phases for which each will be responsible.

(3) Additional Personnel

List names, titles, and proposed duties of additional personnel, if any, who will be required for full-time employment, or on a subcontract or consultant basis. The technical areas, character, and extent of subcontract or consultant activity will be indicated and the anticipated sources will be specified and qualified. For all proposed personnel who are not currently members of the offeror's staff, a letter of commitment or other evidence of availability is required. A resume does not meet this requirement. Commitment letters for use of consultants and other personnel to be hired must include:

-The specific items or expertise they will provide.
-Their availability to the project and the amount of time anticipated.
-Willingness to act as a consultant.
-How rights to publications and patents will be handled.

(4) Resumes

Resumes of all key personnel are required. Each must indicate educational background, recent experience, specific or technical accomplishments, and a listing of relevant publications.

(2) **Technical Evaluation**

Proposals will be technically evaluated in accordance with the factors, weights, and order of relative importance as described in the TECHNICAL EVALUATION FACTORS FOR AWARD.

(3) **Additional Technical Proposal Information**

a) Proposals which merely offer to conduct a program in accordance with the requirements of the Government's scope of work will not be eligible for award. The offeror must submit an explanation of the proposed technical approach in conjunction with the tasks to be performed in achieving the project objectives.

b) The technical evaluation is conducted in accordance with the weighted technical evaluation criteria by an initial review panel. This evaluation produces a numerical score (points) which is based upon the information contained in the offeror's proposal only.

(4) **Other Considerations**

Record and discuss specific factors not included elsewhere which support your proposal. Using specifically titled subparagraphs, items may include:

a) Any agreements and/or arrangements with subcontractor(s). Provide as much detail as necessary to explain how the statement of work will be accomplished within this working relationship.

b) Unique arrangements, equipment, etc., which none or very few organizations are likely to have which is advantageous for effective implementation of this project.

c) Equipment and unusual operating procedures established to protect personnel from hazards associated with this project.

d) Other factors you feel are important and support your proposed research.

e) Recommendations for changing reporting requirements if such changes would be more compatible with the offeror's proposed schedules.

(5) **Information Technology Systems Security**

If this project involves Information Technology, the proposal must present a detailed outline of its proposed Information Technology systems security program which complies with the requirements of the Statement of Work, the Computer Security Act of 1987 Office of Management and Budget (OMB) Circular A-130, Appendix III, "Security of Federal Automated Information Systems," and the DHHS Automated Information Systems Security Program Handbook (Release 2.0, dated May, 1994). The proposal will also need to include similar information for any subcontract proposed.

NOTE: OMB A-130 is accessible via web site: http://www.whitehouse.gov/WH/EOP/OMB/html/circular.html

c. **BUSINESS PROPOSAL INSTRUCTIONS** [Return to Table of Contents]

(1) **Basic Cost/Price Information**

The business proposal must contain sufficient information to allow the Government to perform a basic analysis of the proposed cost or price of the work. This information shall include the amounts of the basic elements of the proposed cost or price. These elements will include, as applicable, direct labor, fringe benefits, travel, materials, subcontracts, purchased parts, shipping, indirect costs and rate, fee, and profit.

(2) **Proposal Cover Sheet**

a) The following information shall be provided on the first page of your pricing proposal:

1. Solicitation, contract, and/or modification number;
2. Name and address of Offeror;
3. Name and telephone number of point of contact;
4. Name, address, and telephone number of Contract Administration Office, (if available);
5. Name, address, and telephone number of Audit Office (if available);
6. Proposed cost and/or price; profit or fee (as applicable); and total;
7. The following statement: By submitting this proposal, the offeror, if selected for discussions, grants the contracting officer or an authorized representative the right to examine, at any time before award, any of those books, records, documents, or other records directly pertinent to the information requested or submitted.
8. Date of submission; and
9. Name, title and signature of authorized representative.

This cover sheet information is for use by offerors to submit information to the Government when cost or pricing data are not required but information to help establish price reasonableness or cost realism is necessary. Such information is not considered cost or pricing data, and shall not be certified in accordance with FAR 15.406-2.

b) The information submitted shall be at the level of detail described below.

1. **Direct Labor**

Provide a time-phased (e.g., monthly, quarterly, etc.) breakdown of labor hours, rates, and cost by appropriate category. Key personnel will be separately estimated as above and identified. Give the basis for the estimates in each case.

2. **Materials**

Provide a consolidated price summary of individual material quantities included in the various tasks, orders, or contract line items being proposed and the basis for pricing (vendor quotes, invoice prices, etc.).

3. **Subcontracted Items**

Include parts, components, assemblies, and services that are to be produced or performed by others in accordance with offeror's design, specifications, or direction and that are applicable only to the prime contract. For each subcontract over $500,000, the support should provide a listing by source, item, quantity, price, type of subcontract, degree of competition, and basis for establishing source and reasonableness of price, as well as the results of review and evaluation of subcontract proposals when required by FAR 15.806.

4. **Raw Materials**

Consists of material in a form or state that requires further processing. Provide priced quantities of items required for the proposal.

5. **Purchased Parts**

Includes material items not covered above. Provide priced quantities of items required for the proposal.

6. **Fringe Benefits**

Show fringe benefits as a separate line item. Include the rate(s) and/or method of calculating fringe benefits. Provide a copy of your fringe benefit rate or institutional guidelines.

7. **Indirect Costs**

Indicate how offeror has computed and applied offeror's indirect costs, including cost breakdowns, and provide a basis for evaluating the reasonableness of proposed rates. Indicate the rates used and provide an appropriate explanation. Where a rate agreement exists, provide a copy.

8. **Special Equipment**

If direct charge, list any equipment proposed including description, price, quantity, total price, purchase or lease, and the basis for pricing.

9. **Travel**

Provide the cost of travel including destination, duration, purpose, per diem, transportation, and the basis for pricing.

10. **Other Costs**

List all other costs not otherwise included in the categories described above (e.g., computer services, consultant services) and provide basis for pricing.

To assist in the preparation of future cost estimates, the Projected Consumer Price Index may be accessed at: http://amb.nci.nih.gov/cpi.htm

(3) **Qualifications of the Offeror**

a) You are requested to submit a summary of your "General Experience, Organizational Experience Related to this RFP, Performance History and Pertinent Contracts."

(1) **General Experience**

General experience is defined as general background, experience and qualifications of the offeror. A discussion of proposed facilities which can be devoted to the project may be appropriate.

(2) **Organizational Experience Related to the RFP**

Organizational experience is defined as the accomplishment of work, either past or on-going, which is comparable or related to the effort required by this RFP. This includes overall offeror or corporate experience, **but not** the experience and/or past performance of individuals who are proposed as personnel involved with the Statement of Work in this RFP.

(3) **Performance History**

Performance history is defined as meeting contract objectives within delivery and cost schedules on efforts, either past or on-going, which is comparable or related to the effort required by this RFP.

(4) **Pertinent Contracts**

Pertinent contracts is defined as a listing of each related contract completed within the last three years or currently in process. The listing should include: 1) the contract number; 2) contracting agency; 3) contract dollar value; 4) dates contract began and ended (or ends); 5) description of contract work; 6) explanation of relevance of work to this RFP; 7) actual delivery and cost performance versus delivery and cost agreed to in the contract(s). For award fee contracts, separately state in dollars the base fee and award fee available and the award fee actually received. The same type of organizational experience and past performance data should be submitted.

(5) **Pertinent Grants**

List grants supported by the Government that involved similar or related work to that called for in this RFP. Include the grant number, involved agency, names of the grant specialist and the Science Administrator, identification of the work, and when performed.

You are cautioned that omission or an inadequate or inaccurate response to this very important RFP requirement could have a negative effect on the overall selection process. Experience and past performance are factors which are relevant to the ability of the offerors to perform and are considered in the source selection process.

(4) **Other Administrative Data**

a) **Property**

(1) It is DHHS policy that Contractors will provide all equipment and facilities necessary for performance of contracts. Exception may be granted to furnish Government-owned property, or to authorize purchase with contract funds, only when approved by the Contracting Officer. If the offeror is proposing that the Government provide any equipment, other than that specified under Government Furnished Property in the RFP, the proposal must include comprehensive justification which includes:

(a) An explanation that the item is for a special use essential to the direct performance of the contract and the item will be used exclusively for the purpose. Office equipment such as desks, office machines, etc., will not be provided under a contract except under very exceptional circumstances.

(b) No practical or economical alternative exists (e.g., rental, capital investment) that can be used to perform the work.

(2) The offeror shall identify Government-owned property in its possession and/or Contractor titled property acquired from Federal funds, which it proposes to use in the performance of the prospective contract.

(3) The management and control of any Government property shall be in accordance with DHHS Publication (OS) 686 entitled, "Contractor's Guide for Control of Government Property (1990)," a copy of which will be provided upon request.

b) **Royalties**

The offeror shall furnish information concerning royalties which are anticipated to be paid in connection with performance of work under the proposed contract.

c) **Submission of Electronic Funds Transfer Information with Offer, FAR Clause 52.232-38**, (May 1999)

The offeror shall provide, with its offer, the following information that is required to make payment by electronic funds transfer (EFT) under any contract that results from this solicitation. This submission satisfies the requirement to provide EFT information under paragraphs (b)(1) and (j) of the clause at 52.232-34, Payment by Electronic Funds Transfer--Other than Central Contractor Registration.

(1) The solicitation number (or other procurement identification number).
(2) The offeror's name and remittance address, as stated in the offer.
(3) The signature (manual or electronic, as appropriate), title, and telephone number of the offeror's official authorized to provide this information.
(4) The name, address, and 9-digit Routing Transit Number of the offeror's financial agent.
(5) The offeror's account number and the type of account (checking, savings, or lockbox).
(6) If applicable, the Fedwire Transfer System telegraphic abbreviation of the offeror's financial agent.
(7) If applicable, the offeror shall also provide the name, address, telegraphic abbreviation, and 9-digit Routing Transit Number of the correspondent financial institution receiving the wire transfer payment if the offeror's financial agent is not directly on-line to the Fedwire and, therefore, not the receiver of the wire transfer payment.

d) **Financial Capacity**

The offeror shall indicate if it has the necessary financial capacity, working capital, and other resources to perform the contract without assistance from any outside source. If not, indicate the amount required and the anticipated source.

e) **Incremental Funding**

An incrementally funded cost-reimbursement contract is a contract in which the total work effort is to be performed over a multiple year period and funds are allotted, as they become available, to cover discernible phases or increments of performance. The incremental funding technique allows for contracts to be awarded for periods in excess of one year even though the total estimated amount of funds expected to be obligated for the contract are not available at the time of the contract award. If this requirement is specified elsewhere in this RFP, the offeror shall submit a cost proposal for each year. In addition, the following provisions are applicable:

HHSAR 352.232-75, Incremental Funding (January 2001)

(a) It is the Government's intention to negotiate and award a contract using the incremental funding concepts described in the clause entitled Limitation of Funds. Under the clause, which will be included in the resultant contract, initial funds will be obligated under the contract to cover the first year of performance. Additional funds are intended to be allotted to the contract by contract modification, up to and including the full estimated cost of the contract, to accomplish the entire project. While it is the Government's intention to progressively fund this contract over the entire period of performance up to and including the full estimated cost, the Government will not be obligated to reimburse the Contractor for costs incurred in excess of the periodic allotments, nor will the Contractor be obligated to perform in excess of the amount allotted.

(c) The Limitation of Funds clause to be included in the resultant contract shall supersede the Limitation of Cost clause found in the General Provisions.

(End of provision)

f) **Facilities Capital Cost of Money**, FAR 52.215-16, (October 1997)

(This is applicable if you are a commercial organization.)

(b) Facilities capital cost of money [(see FAR 15.408(h)] will be an allowable cost under the contemplated contract, if the criteria for allowability in subparagraph 31.205-10(a)(2) of the Federal Acquisition Regulation are met. One of the allowability criteria requires the prospective Contractor to propose facilities capital cost of money in its offer.

(c) If the prospective Contractor does not propose this cost, the resulting contract will include the clause Waiver of Facilities Capital Cost of Money.

(End of Provision)

If the offeror elects to claim this cost, the offeror shall specifically identify or propose it in the cost proposal for the contract by checking the appropriate box below.

[ ] The prospective Contractor has specifically identified or proposed facilities capital cost of money in its cost proposal and elects to claim this cost as an allowable cost under the contract. Submit Form CASB-CMF (see FAR 31.205-10).

[ ] The prospective Contractor has not specifically identified or proposed facilities capital cost of money in its proposal and elects not to claim it as an allowable cost under the contract.

(5) **Subcontractors**

If subcontractors are proposed, please include a commitment letter from the subcontractor detailing:

a) Willingness to perform as a subcontractor for specific duties (list duties).

b) What priority the work will be given and how it will relate to other work.

c) The amount of time and facilities available to this project.

d) Information on their cognizant field audit offices.

e) How rights to publications and patents are to be handled.

f) A complete cost proposal in the same format as the offeror's cost proposal.

(6) **Proposer's Annual Financial Report**

A copy of the organization's most recent annual report must be submitted as part of the business proposal.

(7) **Representations and Certifications**

One copy of the Representations and Certifications attached as SECTION K shall be completed and be signed by an official authorized to bind your organization. Additionally, a completed copy of the Representations and Certifications shall be submitted from any proposed subcontractor.

(8) **Travel Costs/Travel Policy**

a) **Travel Costs - Commercial**

In accordance with Title II, section 201 of the Federal Civilian Employee and Contractor Travel Expense Act of 1985 (Public Law 99-234), costs for lodging, meals, and incidental expenses incurred by Contractor personnel shall be considered to be reasonable and allowable to the extent they do not exceed on a daily basis the per diem rates set forth in the Federal Travel Regulations, General Services Administration (GSA). Therefore, if travel costs are applicable and proposed by offerors, please be advised that they shall be calculated using the per diem rate schedule as established by GSA. Reimbursement of travel costs under any contract awarded from this RFP shall be in accordance with FAR 31.205-46.

b) **Travel Policy**

One copy of the offeror's (and any proposed subcontractor's) written travel policy shall be included in the business proposal (original only). If an offeror (or any proposed subcontractor) does not have a written travel policy, the offeror shall so state

[RETURN TO RFP COVER PAGE]